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ROENTGENOLOGICAL DIAGNOSIS

GENERALIZED SUBSEROUS EMPHYSEMA THROUGH A SINGLE PUNCTURE

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FOR a long time air has been utilized as a means of contrast in roentgenology to differentiate tissues and organs situated in media of homogeneous density. The present work has the novelty of showing how emphysemata may be used for diagnosis in organic areas in which, as far as I know, the method has not been employed before as, for example, in the cellular tissue of the parametrium or pneumoparametrium, in the retropneumoperitoneum, etc. It is also a novelty insofar as with a single puncture a diffuse and extensive emphysema can be produced over the cellular tissues of the entire body. The question naturally arises as to how an emphysema can be obtained with a single puncture, in the pelvic subperitoneal tissue, in the abdominal subperitoneal layer, in the mediastinum and in the cervical region or the cellular tissue which surrounds the great neurovascular sheaths of the upper and lower limbs. Up to the present, clinicians and radiologists who have utilized gases to furnish contrast media have done so with a localized criterion. The joints have been injected with a view to obtaining a pneumoarthrography, also the peritoneal cavity to obtain a pneumoperitoneum, the perirenal fat to outline the kidney, the pleural space, etc.

In order to carry out this procedure it is necessary to take into account certain anatomical facts. Anatomists are apt to underestimate the importance of the subserous cellular tissue perhaps on account of its not having a definite shape, its function being to fill in certain spaces, and they have not properly realized that these cellular tissues, pelvic, abdominal, thoracic, cervical and the deep tissues of the limbs, are all intercommunicating. They tend to schematize, to describe partitions and folds of fascia, and have given us the not quite true impression that the body is divided up into compartments which hardly communicate with one another.

These compartments when they do exist, have multiple weak points, regions where the cellular tissue of one section is continuous with that of another. Where true compartments really exist they are divided by weak or incomplete membranes, so imperceptible that some anatomists describe them while others deny their existence.

We shall attempt to describe briefly, and only insofar as it concerns the present work

the ample subserous cellular tissue starting in the region of the pelvis. If we take a horizontal section across the sacrum and

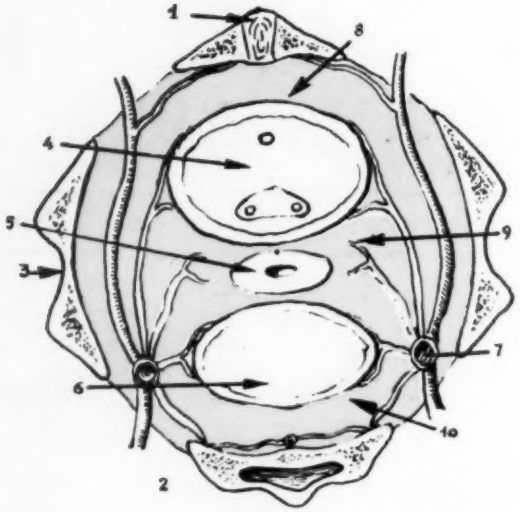

FIG. 1. *1*, pubis; *2*, sacrum; *3*, iliac bone; *4*, bladder; *5*, uterus; *6*, rectum; *7*, hypogastric artery; *8*, paracystium; *9*, parametrium; *10*, paraproctium.

pubis (Fig. 1) we note that the cellular tissue (shown in yellow) fills up the spaces enclosed within the female pelvic wall and the organs situated within: bladder, uterus and rectum. Each organ is surrounded by its own fatty covering called respectively paracystium, parametrium and paraproctium. Besides these the anatomists describe multiple compartments bounded by fascie fibrous laminae and blood vessels which are of certain anatomical interest but which

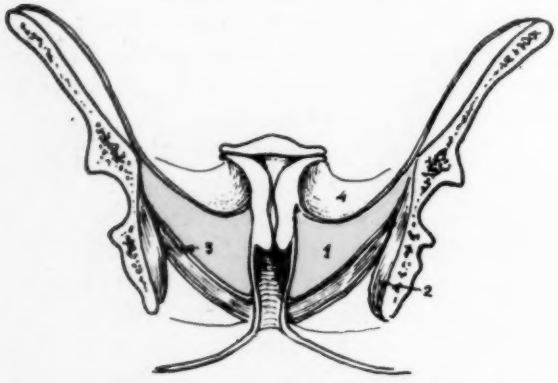

FIG. 2. *1*, parametrium; *2*, levator ani; *3*, visceral deflection of aponeurosis; *4*, peritoneum.

do not form true compartments in the sense that they can retain an emphysema in one space without its passing on to its neighboring space.

In a frontal section (Fig. 2) we can appreciate the amplitude of the cellular tissue in the parametrium. It fills up the space which exists between the levatorani and the peritoneum.

In a horizontal section (Fig. 3) we note how the retrorectal space forms part of the paraproctium and communicates in its upper part with the subperitoneal cellular tissue and how it can go on doing so with other organs enclosed in the mesentery.

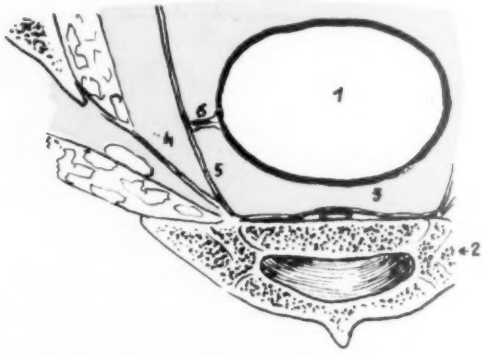

FIG. 3. *1*, rectum; *2*, sacrum; *3*, retrorectal space; *4*, laterorectal space; *5*, sacro-recto-genito-pubic aponeurosis; *6*, rectal wing.

Just as in its posterior aspect the lateral and anterior cellular tissue of the pelvis communicates directly with the lateral and anterior abdomino-subperitoneal tissue.

In a sagittal section (Fig. 4) we can appreciate how the cellular tissue occupies all the space situated between the abdominal wall and the parietal peritoneum, and that this space is very ample in certain regions and that it is continuous, along the mesenteries, with the mesenteric cellular tissue. Either in a direct manner or along the corresponding mesenteries the cellular tissue is in direct relationship with the kidneys (Fig. 5), suprarenal capsules, liver, spleen, pancreas, great vessels, nerves, lymph nodes, nerve ganglia and plexi. The arrangement of the cellular tissue is particularly interesting at the level of the

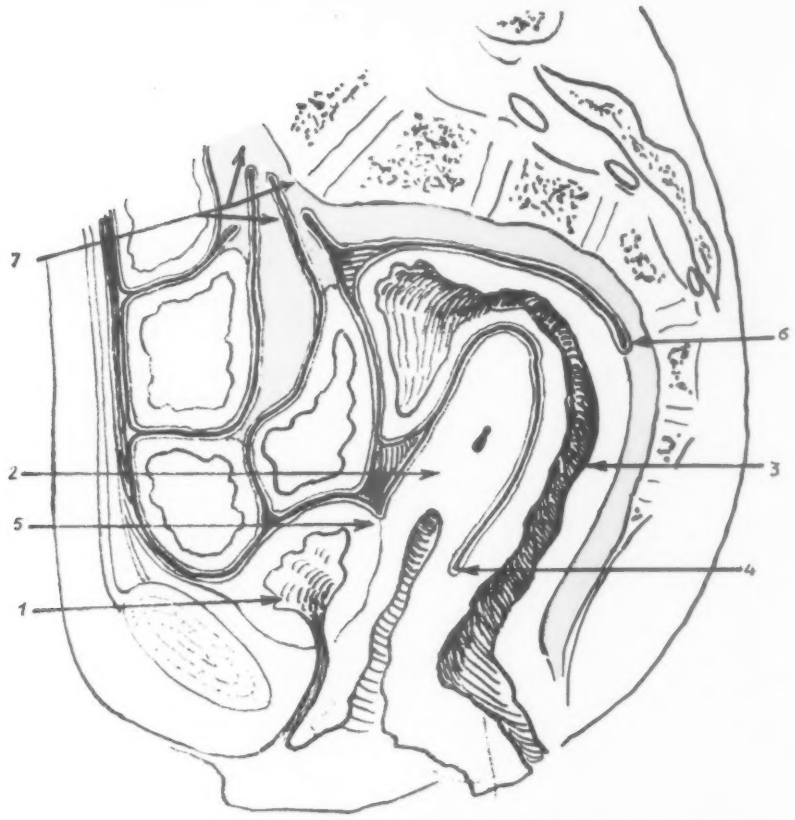

Fig. 4. *1*, bladder; *2*, uterus; *3*, rectum; *4*, rectovaginal sac; *5*, vesicovaginal sac; *6*, sacroretrorectal sac; *7*, mesenteric roots.

posterior abdominal wall and it is convenient to study this particularity in order to be able to explain the difference which exists between the retropneumoperitoneum and the pneumokidney. Between the abdominal wall and the peritoneum we find the renal fascia which forms a cul-de-sac, closed in on all sides except its lower extremity where there exists an ample aperture communicating with the retroperitoneal tissue (Fig. 6 and 7). In renal ptosis this fascia prevents all dislodgment except in a downward direction. The cellular tissue is divided by the renal fascia into two portions: the extrafascial or true retroperitoneal tissue and, within the latter, but separated by the cul-de-sac already mentioned, the intrafascial or perinephric fat. In pneumokidney the emphysema which arises is intrafascial by virtue of

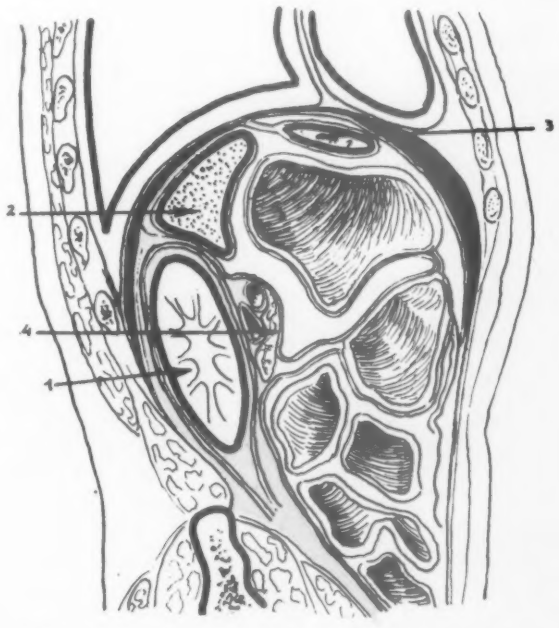

Fig. 5. *1*, kidney; *2*, spleen; *3*, liver; *4*, pancreas.

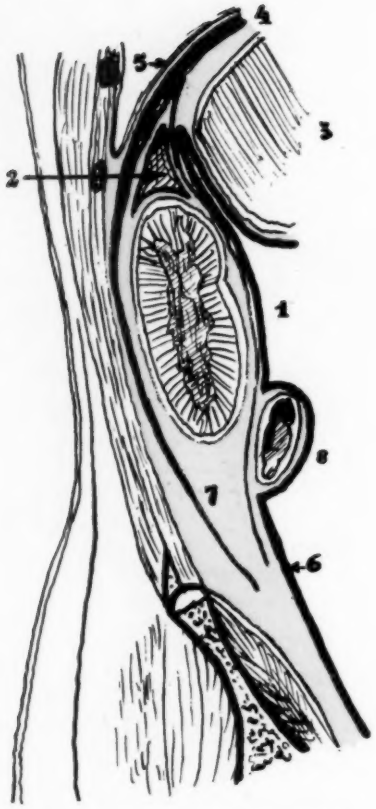

FIG. 6. *1*, kidney; *2*, suprarenal capsule; *3*, liver; *4*, diaphragm; *5*, pleura; *6*, peritoneum; *7*, renal fascia with inferior outlet; *8*, retroperitoneal colon.

which fact the emphysema remains localized around the perinephric fat, and, because this space does not communicate with the corresponding contralateral one, it is necessary in order to demonstrate the other

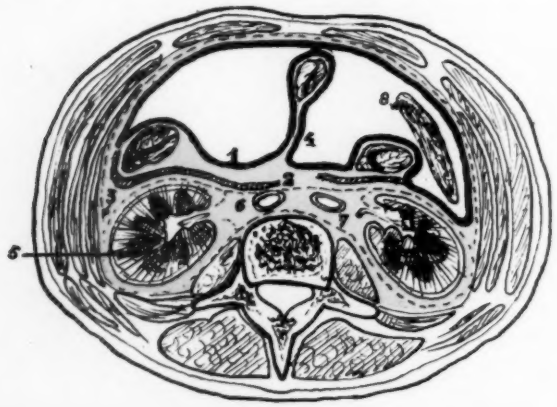

FIG. 7. *1*, peritoneum; *2*, Told's fascia; *3*, fascia propia; *4*, mesentery; *5*, left kidney; *6*, aorta; *7*, vena cava; *8*, liver.

kidney to carry out a second injection to produce the corresponding emphysema. Our technique has the advantage that the emphysema, as it arises along the retrorenal tissue, infiltrates it but because it penetrates the ample inferior opening of the perirenal space one obtains a perirenal emphysema on both sides. In view of the fact that the emphysema produced by a single puncture spreads all over the retroperitoneal tissue one can demonstrate the liver, spleen and portions of the small and large intestines along their corresponding mesenteries.

The retroperitoneal tissue communicates with the mediastinal and subpleural cellular tissue through the weak regions of the diaphragm. Figure 8 is a schematic repre-

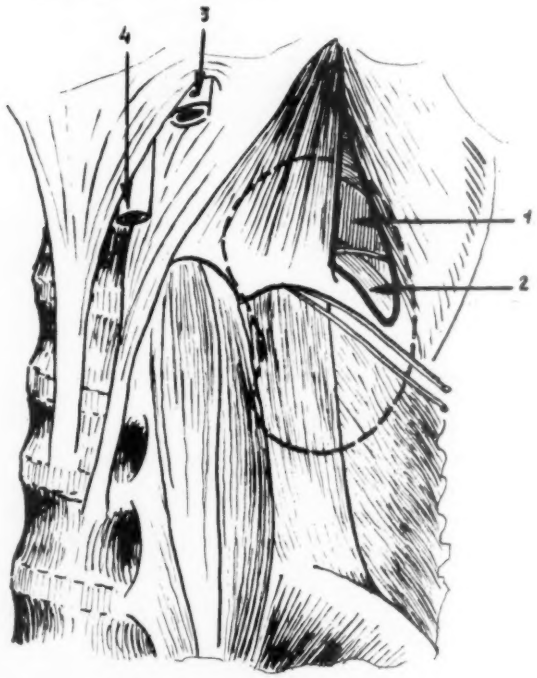

FIG. 8. *1*, pleura; *2*, eleventh and twelfth ribs; *3*, esophagus; *4*, aorta.

sentation of the above mentioned communication through the diaphragmatic hiatus where the pleura and peritoneum come into direct relationship. In the same manner, the cellular tissues surrounding the great vessels and the esophageal hiatus allow the retroperitoneal emphysema to cross the diaphragm to become subpleural

or mediastinal (Fig. 9). Around the periphery of the diaphragm the abdominal cellular tissue communicates with the thoracic cavity across the irregular spaces formed

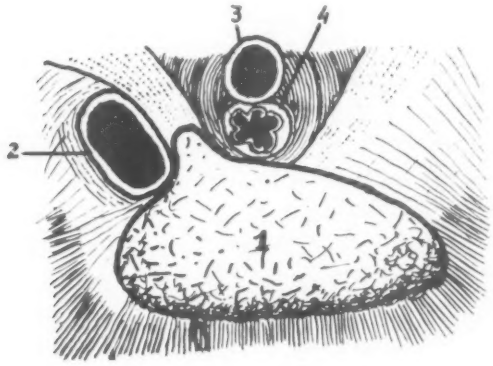

Fig. 9. *1*, region of pericardial attachment; *2*, vena cava; *3*, aorta; *4*, esophagus.

by the fibrous insertions of the diaphragm around its ample periphery. An example of this is afforded by the insertion of the diaphragm to the sternum (Fig. 10) where the fibrous fasciculi leave spaces which are filled by cellular tissue which would be difficult to describe as belonging to either the thorax or the abdomen.

It is true that the existing communication between the abdominal cellular tissue

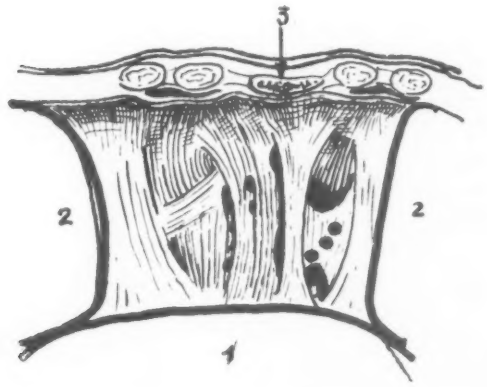

Fig. 10. *1*, pericardium; *2*, pleura; *3*, sternum.

and that of the thorax across the diaphragm and its insertions is not as ample as that existing between the abdomen and the pelvis, yet it is sufficiently ample to allow a retroperitoneal emphysema to rise from the abdomen and become subpleural or mediastinal.

Figure 11 represents schematically a horizontal section at the level of the tracheal bifurcation and in it we see the wide mediastinal space, great vessels, trachea, esophagus and subpleural space. In the same manner, but somewhat exaggerated in the drawing, we have demonstrated the communication between the cellular tissue (mediastinal) and the extradural space across the intervertebral spaces and along

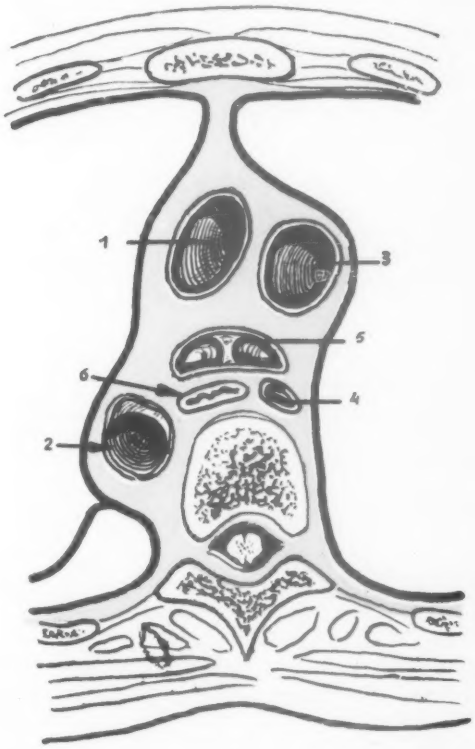

Fig. 11. *1*, ascending aorta; *2*, descending aorta; *3*, superior vena cava; *4*, azygos major; *5*, tracheal bifurcation; *6*, esophagus.

the cellular tissue which accompanies the nerve roots.

The communication between the mediastinal and subpleural cellular tissues and that of the cervical region cannot be doubted by anyone as it would be almost impossible to point out the level at which it ceases to be thoracic cellular tissue to become cervical. Figures 12 and 13 repre-

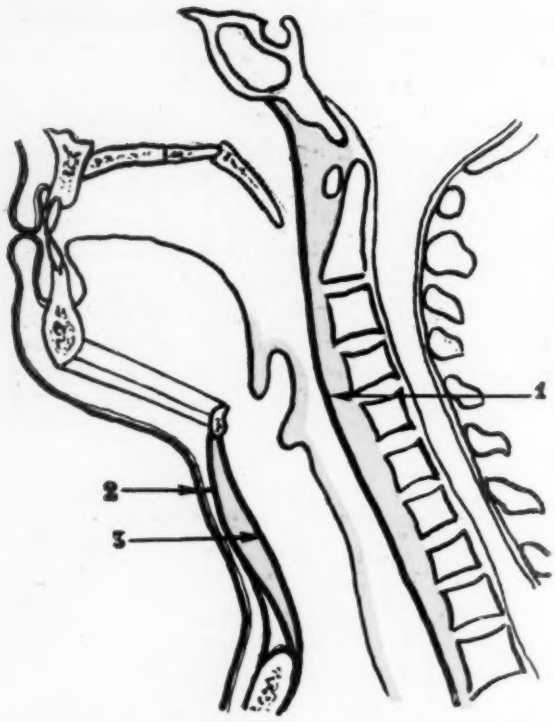

FIG. 12. *1*, deep cervical fascia; *2*, superficial cervical fascia; *3*, mid-cervical fascia.

sent a sagittal and horizontal section of the cervical region.

There is also an obvious communication between the cellular tissue of the pelvic girdle and the upper limbs along the cellular tissue which accompanies the great neurovascular trunks of the arms and the legs.

It is obvious, then, that there is an anatomical continuity of the deep cellular tissue of all the body and that it is possible, by means of the institution of emphysema at certain levels, that this can be made to spread all over the body. There is no doubt that the tissue which lends itself best for the purposes of emphysema is that of the pelvic region and within the pelvis we select the pararectal tissue towards its posterior aspect because of its accessibility, its ample communication with the retroperitoneal tissue and, finally, because of the tendency of all gaseous infiltration to climb upward.

Technique. Point of entry or puncture: at the level of the sacrococcygeal joint, 1 or 2 cm. beyond the inferior border of the sacrum. The needle is directed obliquely upward, inward and forward in such a way that the point of the needle comes to rest in the presacral cellular tissue or the retrorectal space as near as possible to the anterior surface of the sacrum and in its midline.

Of all the tissues traversed by the needle —skin, subcutaneous cellular tissue, aponeurosis, deep cellular tissue—the most highly vascularized is the skin and therefore the danger of emboli is very remote. However, in order to avoid mistakes it is

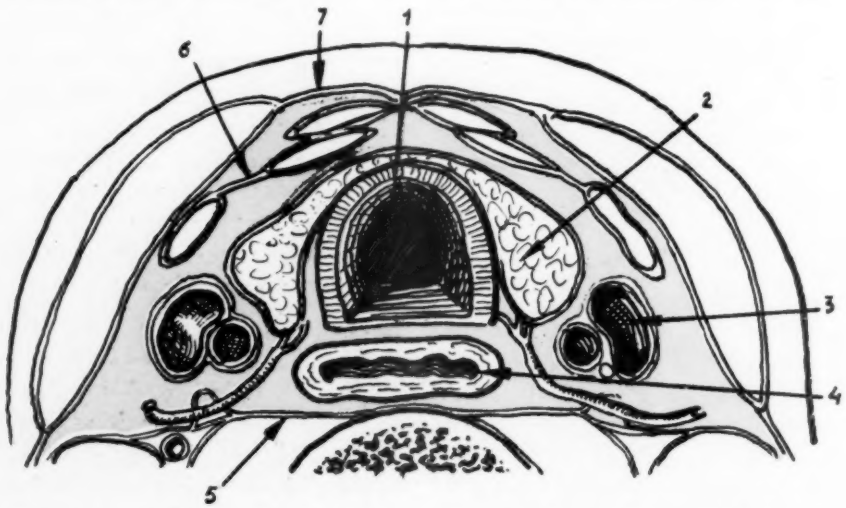

FIG. 13. *1*, trachea; *2*, thyroid gland; *3*, neurovascular bundle; *4*, esophagus; *5*, deep cervical fascia; *6*, mid-cervical fascia; *7*, superficial cervical fascia.

necessary to confirm that the needle is placed within the pararectal tissue and outside a blood vessel. All that is required is to aspirate with a syringe. In none of our cases have we withdrawn blood. On aspirating one can appreciate a negative pull due to the vacuum created by the piston. This pull begins to disappear as air enters the syringe through the connections of needle and syringe. If blood is not withdrawn we then inject a few cubic centimeters of air without moving the needle.

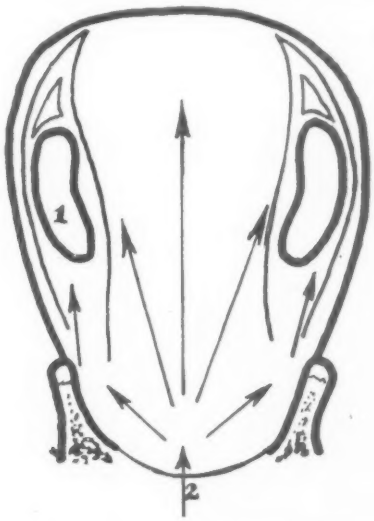

Fig. 14. This diagram shows how a bilateral perirenal emphysema can be obtained with a single injection of gas.

If this injection can be made with ease it is certain that the insufflation will be successful. Should it be necessary to apply considerable pressure to the piston, and air is heard escaping, it is a sign that the needle is situated within very dense cellular tissue and therefore not suitable for gaseous injection. In this case the position of the needle must be altered and this is achieved by advancing it slightly, rarely by removing it altogether.

Position. Any position will do but we prefer the genupectoral.

Gas. The ideal gas would be one which does not exist in the body as in that case we would be assured of its rapid elimination, and it should also be as diffusible as possible to facilitate its infiltration. As we

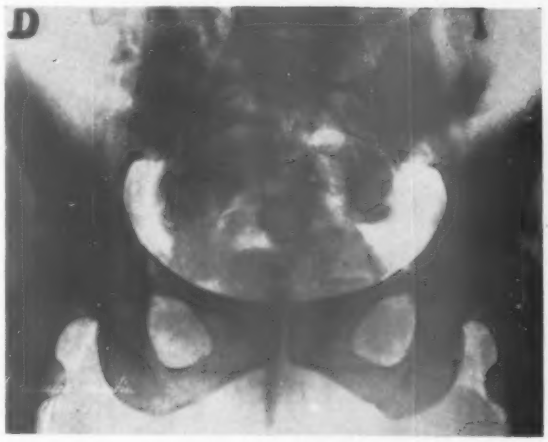

Fig. 15. Pneumoparametrium. Both ovaries are perfectly visible.

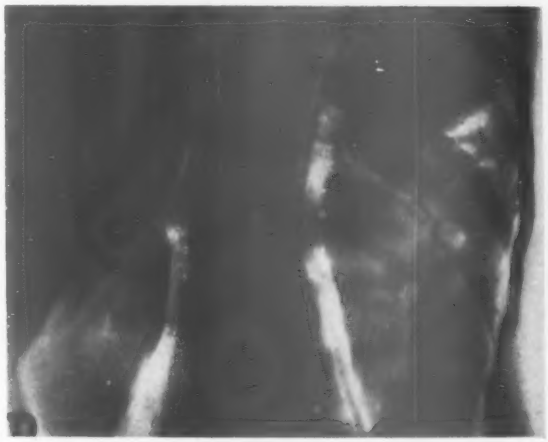

Fig. 16. Retropneumoperitoneum. Both kidneys, adrenals and the hepatic border are seen. Diaphragmatic ligamentous attachments on the lumbar spine, spleen.

Fig. 17. Both kidneys, adrenal glands and inferior border of the liver are well outlined.

FIG. 18. Lateral view of the kidney.

have nothing better available we employ pure oxygen.

Path Followed by the Gas. Once the initial gaseous space is obtained in the pararectum the emphysema advances toward the neighboring pelvic spaces following the paths of least resistance. Its diffusion is ruled exclusively by physical factors some of which are modifiable while others are not. Among these factors are the laxity of the cellular tissue, the position of the subject, the abdominal pressure, the anatomical details, etc.

Professor Botella Llusiá has given this pelvic emphysema the name of "pneumoparametrium." The emphysema surrounds the uterus, tubes, ovaries and, in pathological states, shows up clearly any defects referred to the outer surface, such as adhesions between these organs and the pelvic wall.

The pelvic emphysema ascends into the abdominal cavity by virtue of the continuity of the cellular tissue and infiltrates the space lying between the abdominal wall and the parietal peritoneum. In an ordinary roentgenogram we can appreciate clearly the limits between the subcutaneous cellular tissue and the abdominal wall and if we obtain the limits between the muscular wall and the deep cellular tissue we obtain a picture of all the planes of the abdominal wall.

Of all the abdominal cellular tissue undoubtedly that which offers most interest is the one situated in its posterior wall. Due to the importance of this space we have coined the name "retropneumoperitoneum" for the emphysema which arises in this region. The retropneumoperitoneal space is distinct from the pneumorenal space in that in the latter the emphysema lies within the renal fascia while in the retropneumoperitoneum the emphysema is complete and tends to spread out, as in pneumokidney and, apart from this, along all the cellular tissue which lies between the renal fascia and the abdominal wall and between

FIG. 19. Lateral projection of the kidney.

this and the peritoneum and in the fatty tissue lying above and below the renal fascia. As the emphysema ascends along the paraproctium it does so in all directions (see Fig. 14) and penetrates the inferior aperture of the renal fascia outlining the kidneys and suprarenal glands. Whether or not the suprarenals will be shown up separately from the renal shadow will depend on whether the oxygen will permeate into the cellular tissue separating these organs. When they are firmly adherent without any intervening space it is more than useless to attempt to show them, but as this condition is uncertain we should try to demonstrate a separation between them by means of pressure during roentgenoscopy, at the same time telling the patient to take deep breaths.

We have not as yet succeeded in obtaining an outline of the pancreas and this suggests that there must be certain anatomical reasons which prevent peripancreatic infiltration. On the other hand, the liver and spleen are systematically and totally revealed. A fairly homogeneous emphysema is obtained between the muscular wall and the parietal peritoneum and, on occasions, due to the advancing emphysema across the spaces left free by the visceral peritoneum as it is deflected upon itself, an emphysema is obtained between the capsule surrounding the parenchyma and the visceral peritoneum (in one case the gallbladder was shown). It is somewhat more difficult to show the retroperitoneal large intestine, the large intestine with mesentery and the small intestine. In the first instance the emphysema surrounds the intestine directly while in the second it has to do so across the mesentery.

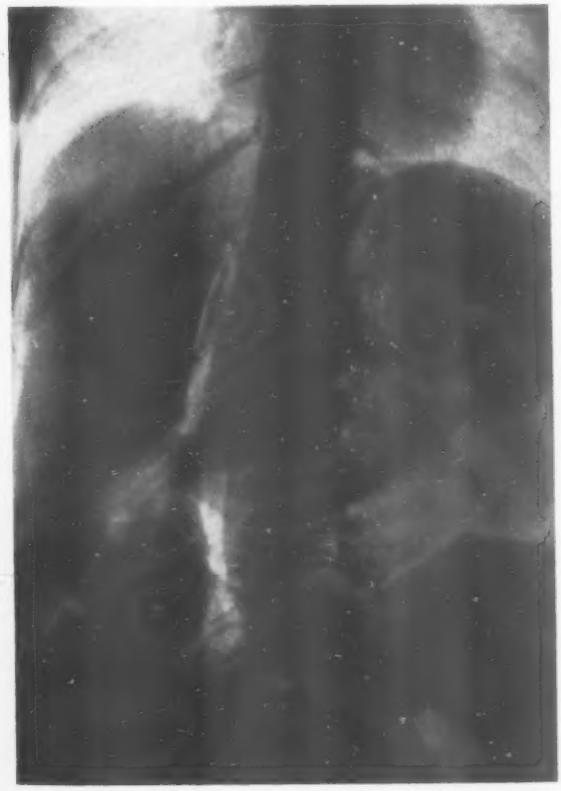

Fig. 20. Both kidneys are ectopic. Hepatomegaly displacing the right kidney and the adrenal gland. Insertions of the diaphragm on the lumbar spine. Splenomegaly.

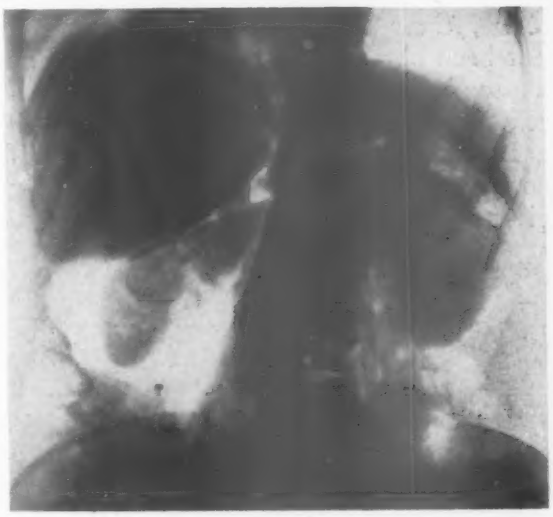

Fig. 21. Right kidney displaced by the liver. Stone in the gallbladder. No contrast medium as used in cholecystography has been employed.

The psoas muscle, which is usually visible in plain roentgenograms of the abdomen, stands out much more clearly because its borders acquire an unsuspected clearness due to the retropneumoperitoneum.

The diaphragm is outlined clearly and it is curious to note the precision with which part of its insertions to the lumbar spine are shown, as is also its central or aponeurotic portion which can be seen separated from the pericardium. As far as we

know, these roentgenological data have not been obtained up to the present. The anatomical fundamentals of such a possibility have been discussed above.

In the mediastinum the induction of emphysema has no great value as it only gives us more or less the same data as are obtained by ordinary means. Any advantages obtained by the pneumomediastinum are referable only to a sharper outline of the mediastinal contents, without evincing any new images. Contrary to this, in the neck region it is very easy to demonstrate the retroesophageal space, the larynx, the borders of the thyroid gland, and so forth.

The inconveniences afforded by this method are merely those of the actual puncture and are comparable to any other type of puncture. Any inconvenience caused by the emphysema is transient and if pure oxygen is injected it disappears within a few hours.

Before deciding upon the above technique, and due to the fact that we had not thought that there was an anatomical continuity in the deep cellular tissue and had not discovered the fragility of its barriers, we surmounted the first obstacle, the diaphragm, by taking advantage of the multiple foramina in the spinal column. Gas was injected extradurally in the sacral canal and it filled rapidly the free space between the dura and the bony walls so that when it became completely filled it poured out through the divers openings just as air goes through the holes of a flute. In this manner twenty-nine pairs of emphysematous zones were obtained which, on becoming confluent, produced a generalized emphysema. This method, theoretically insuperable, has definite practical defects. The emphysema is obtained with a speed

FIG. 22. Right kidney and superior pole of the left kidney are visible. Large tumor mass on the left side covering the inferior pole of the left kidney. Hepatomegaly. Gallbladder seen without contrast medium. Diaphragm insertions. Fibrous diaphragm separated from the pericardium.

FIG. 23. Detail of the roentgenogram in Figure 22.

which is in proportion to the laxity of the cellular tissue, and because this tissue is very lax in the cervical region the infiltration of gas is more rapid and energetic in this region; the neck increases in volume, the vocal cords become infiltrated and the patient becomes apprehensive when the tone of his voice suddenly becomes deeper. This sign is of no special significance but it is unpleasant for the patient. The emphysema, even when it affects the vocal cords, is quite harmless and the oxygen is eliminated rapidly, passing into the blood stream where part of it is used up and the rest eliminated into the exterior via the lungs. It must be kept in mind that fatal cases of mediastinal and cervical emphysema are due to valvular tears of the mediastinal pleura or to wounds, also valvular, of the progressive accumulation of air until such pressures are reached that the cardio-respiratory function becomes fatally impaired. In induced emphysema, once the injection of gas is finished, the intracellular

Fig. 24. Cecum, right and left colon. Both kidneys, calcified masses over the shadow of the right psoas.

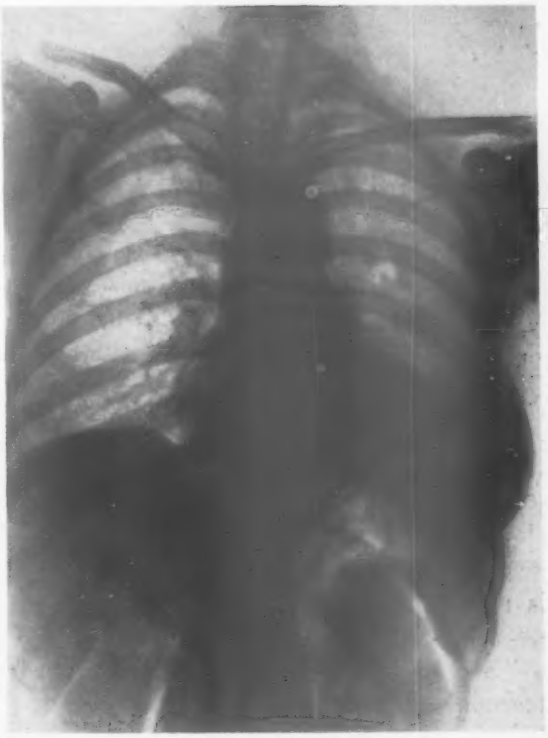

Fig. 25. Fibrous diaphragm separated from the pericardium, spleen, both kidneys, adrenals, mediastinum.

Fig. 26. Pharynx, retroesophageal space, larynx, epligottis, trachea, thyroid.

pressures of the gaseous chamber tend necessarily to descend due to the elimination of gas toward the exterior.

Usually the diagnostic problems which would require the institution of a generalized emphysema arise in the pelvis and abdomen. It would therefore seem unnecessary to inconvenience the patient by infiltrating his mediastinum and cervical region when we can solve the problem by a simpler technique than the extradural. If the problem to be solved is pelvic and the condition of the patient admits, we induce the pneumoparametrium directly through the vagina and if this is not possible we do so through the retrorectal space. With both these techniques we also obtain a thoracic and cervical emphysema but its intensity is minimal compared with that obtained near the site of injection.

To conclude, we can say that this new technique by means of the formation of a subserous emphysema has special indications and facilitates the obtaining of the direct outline of organs and structures which, up till the present had not been shown roentgenologically, such as the uterus, fallopian tubes, ovaries, liver, spleen, the leaves of the diaphragm, the divers cul-de-sacs of the peritoneum, the thyroid gland, and so forth.

It is many years ago that views of the kidneys and suprarenal glands were obtained by means of various pneumatic techniques which differed very slightly from one another. Our technique has important advantages compared with even the best among the many employed up to now:

1. It has the great advantage of requiring only one puncture.

2. The advantage of its innocuousness rests on the fact that the possibility of an embolism is so remote that it need not be taken into account. With our technique it is not possible to damage any parenchymatous tissue and the most vascular tissue which is crossed by the needle is the skin.

3. The anatomical advantages are shown by the fact that if the kidney has descended to outside the limits of the renal fascia it is not possible to demonstrate its presence when using the ordinary pneumatic techniques but with our method it is always demonstrable whatever its situation.

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A ROENTGENOGRAPHIC AID IN THE DIAGNOSIS OF RETINOBLASTOMA

By HAROLD FULTON, M.D.*

DETROIT, MICHIGAN

THE retinoblastoma, the commonest form of retinal glioma, is a malignant tumor occurring mainly in infants and children. Because of the insidious and rapid growth of this tumor, early diagnosis is imperative if the child's life is to be saved. In its advanced stages, typified by a protruding, ecchymotic orbital mass, the clinical diagnosis of malignant tumor of the eye is obvious and roentgenographic studies at this time would only serve to demonstrate the extent of extraocular growth of the neoplasm. In its earliest stages, however, the clinical recognition of the existence of a small retinal tumor is extremely difficult. In fact, it is said[5] that error in clinical diagnosis occurs in one-third of all cases in which the eye is removed for this disease (retinoblastoma). The importance of preservation of the eye, even though sightless, is to be emphasized, as in an infant or child the eye is needed to mold the bony orbit. However, unless the diagnosis of benign disease can be definitely established, enucleation of the affected eye is mandatory. Therefore, any aid that the radiologist could give the ophthalmologist in making a definite diagnosis of retinoblastoma would be welcome.

CLINICAL COURSE

The clinical course of retinoblastoma is usually divided into four stages:[2]

1. Intraocular growth—The tumor begins as a small nodule in the posterior part of the retina. As the tumor enlarges it may grow into the vitreous (endophytum), or outward, detaching the retina (exophytum).

2. Glaucoma—Increased tension eventually intervenes, and owing to the softness of the child's eye, the eye enlarges, most often displaying exophthalmos.

3. Extraocular extension—When the globe becomes filled with tumor, a break in the sclera occurs and, having escaped from the eye, the tumor invades the periorbital structures with amazing rapidity. Usually, before the latter occurs there has been infiltration of the optic nerve.

4. Metastasis—Actual metastasis is said to be rare.[6] Extension into the brain and cranial bones by way of the optic nerves and tracts is very common.

PATHOLOGICAL FEATURES

Without discussing the complex pathological features of these tumors,[4] it can be stated that it is of some importance that degenerative changes, especially calcification, are common. These degenerative areas involve the cells farthest removed from the numerous blood vessels which permeate the tumor. The cells in these regions become necrotic and these areas of necrosis are infiltrated by large phagocytic cells rich in lipoids. It is in these regions that calcium is deposited, even in the earliest tumors.

That retinoblastomas commonly contain areas of calcification of sufficient density and extent to be demonstrable roentgenographically is known to ophthalmologists, but thus far has received little attention from the radiologists. There is no mention of the phenomena in the standard roentgenological texts, and scant reference to the observation in radiological papers, which mainly concern the radiation therapy of the disease.

The popular ophthalmologic textbooks mention the possibility of roentgenographic visualization of a partially calcified tumor within an orbit harboring a retinoblastoma. One author,[3] in discussing retinoblastoma, states that "in a number of cases, x-ray

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examination of the eye reveals islands of calcification in the tumor." Duke-Elder[2] suggests that "radiography may provide a clue. In a large proportion of cases [of retinoblastoma], small islets of calcification are present in the tumor; it is rare for calcareous degeneration to be present in the eye of a child in other circumstances." Friedenwald, in Berens' monograph,[1] remarks that "the roentgen ray examination may occasionally be useful in the differential diagnosis [of retinoblastoma]. The necrotic areas in the tumor are frequently calcified and cast characteristic flaky shadows in the roentgen picture."

The most comprehensive study was made by Pfeiffer[5] in 1936. He found that orbits studied preoperatively by roentgenograms, revealed calcification in 11 of 14 eyes in which retinoblastoma was subsequently diagnosed pathologically. In 2 of the cases in which no calcification was seen, the tumor was very small, but in 1 case in which no calcification in the orbit was demonstrable, the malignant growth filled the entire vitreous cavity. None of the 4 cases of "pseudoglioma" studied contained calcification which could be roentgenographically demonstrated. Pfeiffer concluded that in approximately 75 per cent of cases of retinoblastoma there is sufficient calcareous degeneration to be recognized roentgenographically and that the granular and irregular calcium density shadow thus demonstrated is pathognomonic when found in children.

ROENTGENOGRAPHIC TECHNIQUE

Roentgenograms of good detail are required for the appreciation of small shadows of calcium in a small tumor. Anesthetization of the child should not be necessary for single Caldwell and Waters views; stereoscopic films in these positions are of great value but difficult to obtain. The lateral film or the "bone free" technique, as suggested by Pfeiffer,[5] are not absolutely necessary. Oblique views of the optic foramina are useful to demonstrate extension of the tumor into the optic nerve.

ROENTGEN FEATURES

If the eye is of normal size, or shrunken, a soft tissue mass may not be demonstrable; in protruding tumors, obvious increase in soft tissue mass and density is present in the involved orbit. Whether increased soft tissue mass is present or not, a rounded mass of mottled calcification, representing the partially calcified tumor, may be present in the eye. On careful examination, the globular mass is seen to consist of closely packed, but individual, calcified nodules measuring approximately 1 millimeter in diameter.

Infiltration of the malignancy along the optic nerve is a common event and, in case of such extension, roentgenograms of the optic foramina may reveal definite changes. If the tumor is confined within the dural sheath of the optic nerve, the foramen may be enlarged to several times its normal size. If the sheath of the nerve has been perforated, erosion of the bony walls of the foramen may be seen. The roentgenograms should be carefully examined for these signs, since they indicate extension of the tumor outside of the eye and their presence might alter the plan of treatment.

CASE REPORTS

In the years 1947–1949 inclusive, 4 cases of retinoblastoma were studied preoperatively by roentgenograms at Harper Hospital and Children's Hospital of Michigan. In 3, definite areas of calcification were demonstrable and in all cases calcification was found in the tumor by the pathologist. Two of the cases are presented in detail.

Case 1. G. P., an eleven month old colored female. At seven months of age the parents noted a yellowish-green opacity behind the child's left pupil. This slowly increased in size, but there were no eye symptoms until one day before admission (July 30, 1949), when itching and swelling of the left eye began. The patient was examined by a physician and eye drops were administered. There was no subsequent relief of symptoms and the child was brought to the Children's Hospital of Michigan. On admission to the hospital, examination of the left

eye revealed marked edema and ecchymosis of the upper and lower eyelids on the left, as well as acute conjunctivitis. The admitting diagnosis was blepharitis and possible chemical conjunctivitis. Conservative treatment was employed with success.

The retina of the left eye could not be adequately visualized until five days after admission, when, with the patient under anesthesia, a mass in the left anterior vitreous was seen by ophthalmoscopy. Roentgenograms of the orbits (Fig. 1) on August 8, 1949, revealed "calcification within the left orbit but no evidence of bone destruction." The possibility of calcified retinal hemorrhage was entertained clinically but, partially on the basis of the roentgenograms, the diagnosis of retinoblastoma was made and enucleation of the left eye was performed on August 12, 1949.

Fig. 1. Case 1. Area of calcium density in the midportion of the left orbit.

The pathologic report (W. W. Zuelzer, M.D.) stated that "the vitreous is completely replaced by a homogeneous friable grayish-yellow mass (Fig. 2). This tumor microscopically consists of uniform cells with pink cytoplasm and round or oval nuclei which stain fairly deep blue. Rosettes are evident. There are small areas of degeneration, extravasated blood and *calcification throughout the tumor* (Fig. 3). No malignant cells are in the optic nerve. Diagnosis—retinoblastoma, malignant, left eye."

Case 11. M. J., a six month old white female

Fig. 2. Case 1. Photomicrograph of sectioned left eye (×10), showing the tumor filling the entire vitreous cavity.

(private patient of Dr. L. Carter). At birth the parents noted a light reflected from the pupil of the child's left eye, but were told that the child would outgrow any difficulty. As months passed the parents thought that the whiteness of the object had intensified and, after examination by an oculist, ophthalmologic consultation was obtained.

On admission to Harper Hospital on December 12, 1949, there was noted a white left pupillary reflex, and a fungating growth originating from the temporal side of the left retina was seen by ophthalmoscope. Roentgenograms

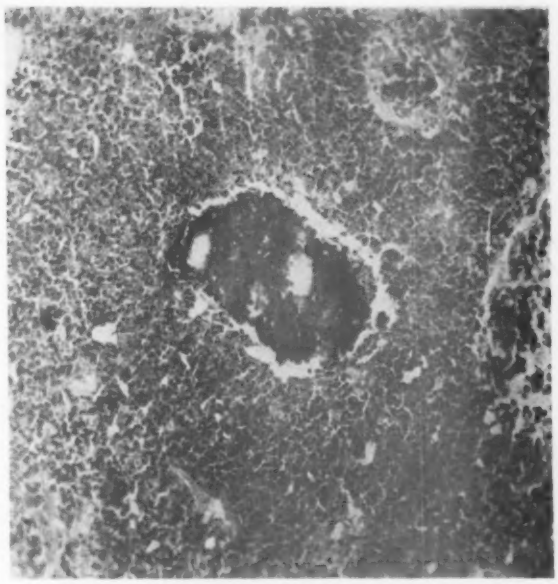

Fig. 3. Case 1. Photomicrograph of sectioned left eye (×200), showing area of calcific degeneration surrounded by typical tumor cells.

of the orbits (Fig. 4) revealed "a considerable amount of amorphous calcification in the region of the ocular body of the left orbit. In a child of this age the findings are virtually pathognomonic of retinoblastoma (glioma)."

FIG. 4. Case II. Mottled area of calcium density in mid-portion of left orbit.

Enucleation of the left eye was performed on December 12, 1949.

The pathologic report (L. E. McCullough, M.D.) stated that "microscopically a mass is seen which fills the globe (Fig. 5), it contains many rosettes, a few sleeves of cells, some thin blood sinuses, *calcium deposits* (Fig. 6), and shows extensive necrosis in areas. There is invasion of the optic nerve head, but no involvement of the optic nerve itself or of the sclera. Diagnosis—retinoblastoma, with invasion of the nerve head."

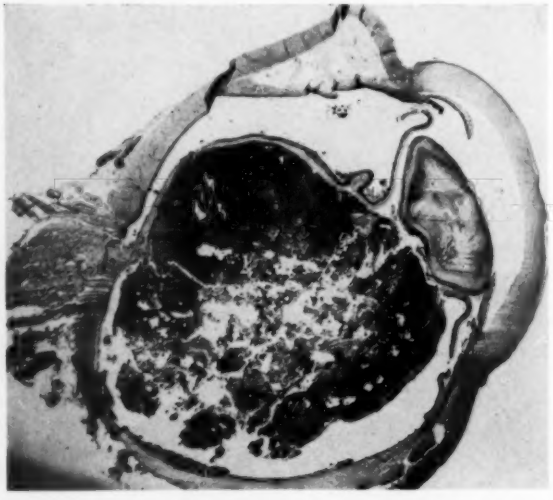

FIG. 5. Case II. Photomicrograph of sectioned left eye (×10), showing tumor arising near nerve head and filling the vitreous cavity.

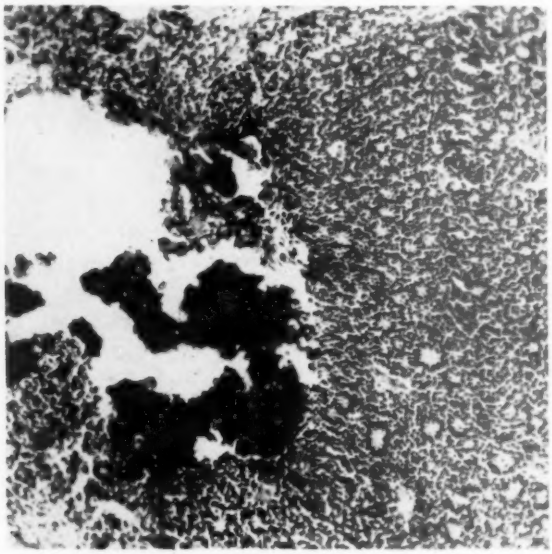

FIG. 6. Case II. Photomicrograph of sectioned left eye (×200), showing large area of calcific degeneration surrounded by typical tumor cells. Numerous rosettes are present.

A postoperative roentgenogram of the enucleated eye visualizes the calcified tumor to advantage (Fig. 7).

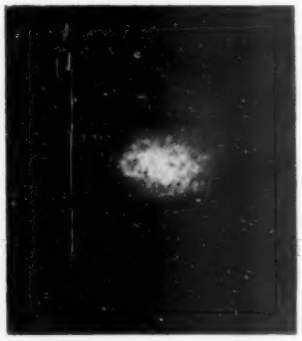

FIG. 7. Case II. Roentgenogram of left eye after enucleation, demonstrating the granular character of the calcification in the tumor.

DISCUSSION

Clinically, several conditions occurring in children may simulate a retinoblastoma and these are usually descriptively grouped together under the term "pseudoglioma."

The most important of the pseudogliomas are:

1. Congenital abnormalities such as retrolental fibroplasia and persistent hyaloid vessel (tunica vasculosa lentis).

2. Retinal detachment with intraocular hemorrhage.

3. Inflammatory conditions such as gumma, tuberculoma, and exudative retinitis. Another, metastatic ophthalmitis, commonly follows a generalized infection such as measles, scarlet fever, whooping cough and meningitis.

4. Angiomatosis of the retina (von Hippel's disease).

5. Cysticercus infestation of the retina.

Ophthalmologists have attempted to derive some basis for differentiation between true and pseudogliomas. The color of the light reflex, eye tension, and appearance of the intraocular mass are but a few of the criteria frequently used and often found inadequate.

The roentgenographic differential involves only a few of the rare conditions, since the congenital abnormalities and the inflammatory conditions almost never contain areas of calcification. Occasionally retinal hemorrhage may include plaques of calcium, and streaks of calcium may be the manifestation of angiomatosis of the retina. The calcified regions in these two conditions, however, in no way resemble the flaky, irregular mass of calcium presented by the retinoblastoma.

CONCLUSIONS

1. Retinoblastoma, the commonest malignant eye tumor of children, very frequently contains calcification in necrotic areas.

2. This calcification can be demonstrated in about 75 per cent of the cases by means of roentgenograms of the orbits.

3. Granular irregular calcification in the orbit of an infant or child is virtually pathognomonic of retinoblastoma.

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ROENTGENOLOGIC ASPECTS OF DIFFUSE MILIARY GRANULOMATOUS PNEUMONITIS OF UNKNOWN ETIOLOGY*

REPORT OF TWELVE CASES WITH EIGHTEEN MONTHS' FOLLOW-UP

By BENJAMIN FELSON, M.D., GEORGE F. JONES, M.D., *and* ROBERT P. ULRICH, M.D.

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FELDMAN and Sabin[8,9] recently reported an outbreak of an unusual illness which occurred in July, 1947, in a group of 12 men who had been engaged in cleaning out an abandoned tower in a Cincinnati public park. The material removed from the tower contained, among other things, a large quantity of wet pigeon excreta. The clinical manifestations, which appeared from five to fourteen days after exposure, varied from a mild, transitory grippe-like syndrome of a few days' duration to a more severe prostrating illness which lasted almost three weeks. Extensive laboratory studies failed to reveal a causative agent. Since small granulomatous lesions were found in the lungs and tracheobronchial lymph nodes of one of the patients, who died of coronary thrombosis five months after the acute illness, Feldman and Sabin designated this disease "diffuse miliary granulomatous pneumonitis."

The most striking feature observed during the epidemic was the pulmonary involvement revealed in roentgenograms of the chest. We have made serial roentgenographic studies on these patients over a period of approximately eighteen months, and the results of these studies are the basis of the present communication.

ROENTGEN FINDINGS

In each case the admission film, which was obtained from five to seven days after onset of symptoms, showed the presence of innumerable finely nodular densities, diffusely and symmetrically distributed throughout the lung fields. On the roentgenograms (Fig. 1*A*, 2*A* and 3*A*), the nodules appeared somewhat more concentrated in the central portions of the lung fields but, as is well known, this type of distribution does not represent the true anatomic distribution of the lesions. The individual nodules varied from 1 to 3 mm. in diameter and were ill defined and noncoalescent (Fig. 2*B* and 3*B*). The appearance was indistinguishable from that seen in miliary tuberculosis.

Hilar and mediastinal lymphadenopathy were not apparent. The bronchovascular markings were normal. There was no evidence of segmental or lobar infiltrate or of pleural involvement.

The roentgen findings in all the cases were remarkably similar, differing only quantitatively. The amount of pulmonary involvement did not reflect the duration of exposure or the severity of symptoms.

Chest films were made at weekly intervals for the first month after admission and at intervals of from one to three months thereafter. On films obtained one week after admission (about two weeks after onset), a slight increase in pulmonary involvement was noted in 5 cases, while no change was detected in the other 7. The subsequent roentgenological course was noted to vary among the cases. In 7 cases the lesions became gradually less perceptible on each succeeding roentgenogram and ultimately faded completely (Fig. 1 and 2). The clearing process took place over a

* From the Department of Radiology, University of Cincinnati College of Medicine and Cincinnati General Hospital. Presented at the Fiftieth Annual Meeting, American Roentgen Ray Society, Cincinnati, Ohio, Oct. 4–7, 1949.

period varying from one to twelve months after onset, most cases showing complete disappearance of the miliary densities between the third and fifth months.

In 4 of the remaining 5 cases progressive but incomplete clearing occurred from the third week to the tenth month after onset peared. In the cases in which complete regression of the lesions occurred, no abnormalities were apparent on the later films.

DISCUSSION

It is well known that diffuse miliary densities in the lungs are found in many

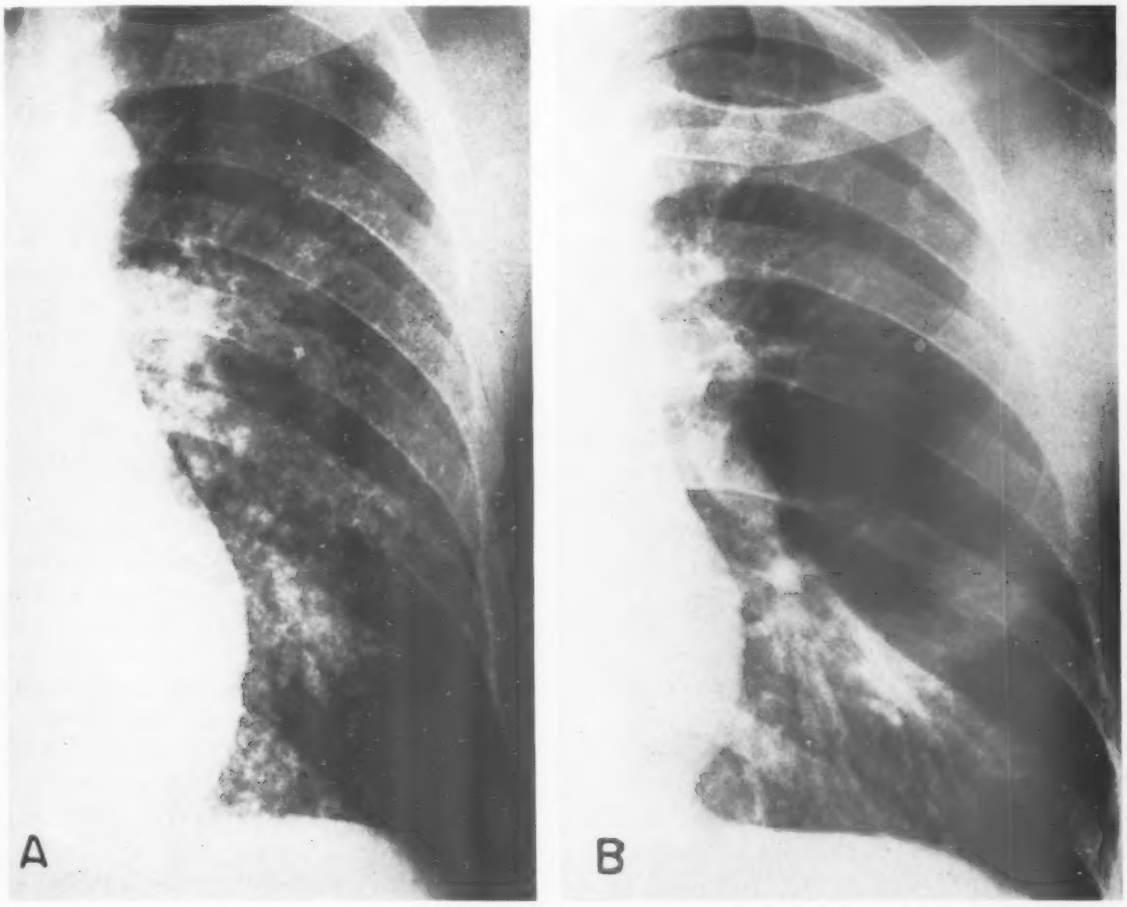

Fig. 1. A. J. Exposed for four days. Onset of symptoms three days later. Severe illness. (*A*) Chest film three weeks after symptoms appeared, showing extensive disseminated miliary densities. (*B*) Chest film three months after onset, showing complete clearing.

(Fig. 3). The process then appeared stationary during the remainder of the follow-up period (eighteen months in 3 cases and fourteen months in 1). The fifth patient showed a similar pattern but died of coronary disease at the end of five months, the last film showing a very faint diffuse pulmonary nodularity.

No evidence of pulmonary calcification, emphysema or cardiac enlargement ap-

diseases. H. Felson and Heublein[10] named approximately eighty different causes of diffuse pulmonary lesions, and Austrian and Brown[1] listed twenty-three conditions in which disseminated miliary lesions are found on roentgenograms of the chest. These authors pointed out that differentiation among these conditions cannot be based on the roentgen appearance alone and that a correct interpretation can only

be accomplished after careful correlation of the roentgenological, clinical and laboratory data. However, the association of other types of intrathoracic involvement such as mediastinal lymphadenopathy, pleural effusion, etc., may be of considerable diagnostic aid. The progression or retrogression of the roentgen changes may also help in establishing the correct diagnosis.

Certain features observed in the cases in this epidemic tend to eliminate a large number of the possibilities listed in the aforementioned articles. These features include:

1. The simultaneous development of an acute febrile illness in a group of men with a common exposure history.
2. The striking similarity of the roentgen changes in all the cases, and the gradual retrogression of these changes.
3. The absence of other intrathoracic manifestations than miliary lesions.
4. The failure to demonstrate an etiologic agent.

There remain, however, a number of diseases which require closer scrutiny, including conditions caused by noxious gases, mycoses, bacteria and viruses. All of these have been known to produce acute febrile illness with miliary lesions in the lungs.

The roentgen appearance in our cases was not that ordinarily encountered following the inhalation of noxious gases, because the pulmonary lesions were much smaller and more discrete than the confluent, flocculent densities usually caused by such gases. Although bronchiolitis obliterans, resulting from the inhalation of certain fumes, may produce diffuse miliary densities on the roentgenogram,[12] the autopsied case failed to reveal such bronchiolar changes. The delay in appearance of clinical manifestations in all the cases would also appear to eliminate noxious gases from consideration.

The possibility that a fungus was responsible for the outbreak merits more serious consideration. It is well known that disseminated miliary lesions can be caused by many of the mycoses.[3,4,6] Although fungus disease of the lungs would be expected to show a greater variation in the roentgen appearance from case to case than was encountered in this series, we feel that the possibility of a mycotic infection has not been completely excluded, although it should be noted that Feldman and Sabin reported negative studies for histoplasmosis, coccidioidomycosis and blastomycosis in these cases.

The same considerations apply to the question of a bacterial etiology. However, in a review of the literature, we could not find a single instance of an epidemic of miliary pneumonia of proved bacterial origin, except that caused by the tubercle bacillus.

A virus etiology was believed likely at the beginning of the outbreak. Ornithosis was strongly suspected because of the abundance of pigeon manure in the building. The possibility of "Q" fever was also considered. Since localized, rather than diffuse pulmonary densities are encountered in these diseases,[7,14,16,18] the roentgenograms did not support either of these diagnoses. They were subsequently ruled out by laboratory studies.[8,9]

The occurrence of diffuse miliary densities in the lungs in primary atypical pneumonia is well known,[13] but we have found no report in which *all* the cases in an epidemic showed this appearance. The prolonged duration of the pulmonary findings also appeared to eliminate primary atypical pneumonia as a diagnostic possibility.

It is possible that some other virus, as yet unidentified, was responsible for the epidemic. To our knowledge, no epidemic of miliary pneumonitis of proved virus etiology has been reported.

Idstrom and Rosenberg,[11] in 1944, reported an epidemic of what they called primary atypical pneumonia which occurred in Camp Crowder, Missouri. Although a larger epidemic was in progress in the camp at the time, the 40 cases they reported were from a single company which had been engaged in cleaning "dusty,

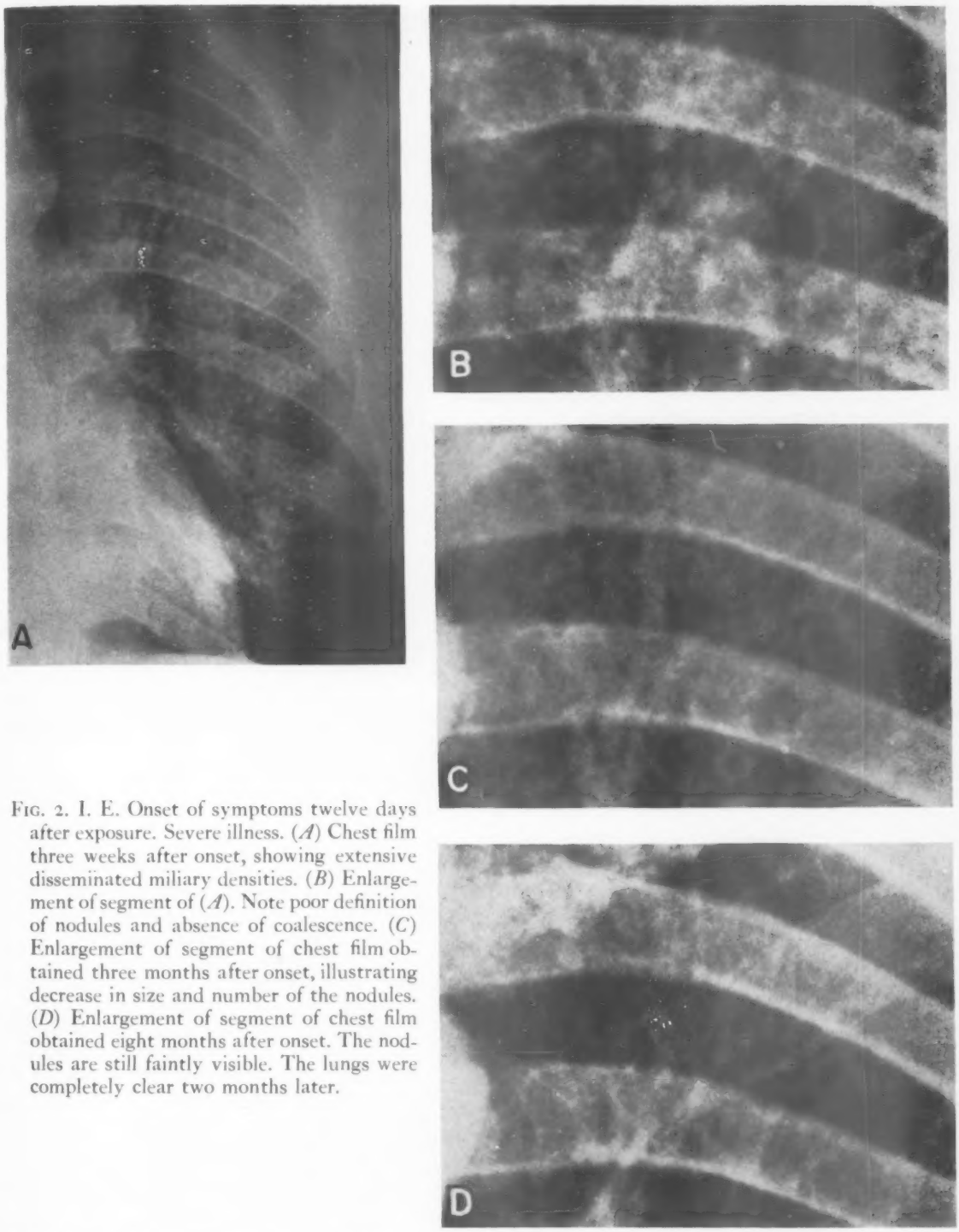

Fig. 2. I. E. Onset of symptoms twelve days after exposure. Severe illness. (*A*) Chest film three weeks after onset, showing extensive disseminated miliary densities. (*B*) Enlargement of segment of (*A*). Note poor definition of nodules and absence of coalescence. (*C*) Enlargement of segment of chest film obtained three months after onset, illustrating decrease in size and number of the nodules. (*D*) Enlargement of segment of chest film obtained eight months after onset. The nodules are still faintly visible. The lungs were completely clear two months later.

abandoned homes, barns, chicken coops and outhouses." The symptoms and signs were those commonly seen in primary atypical pneumonia. Chest films were described as consistently showing patchy peribronchial infiltrations which frequently changed in position. However, the roentgenograms reproduced in this article show disseminated miliary lesions and, except for obvious hilar enlargement, closely re-

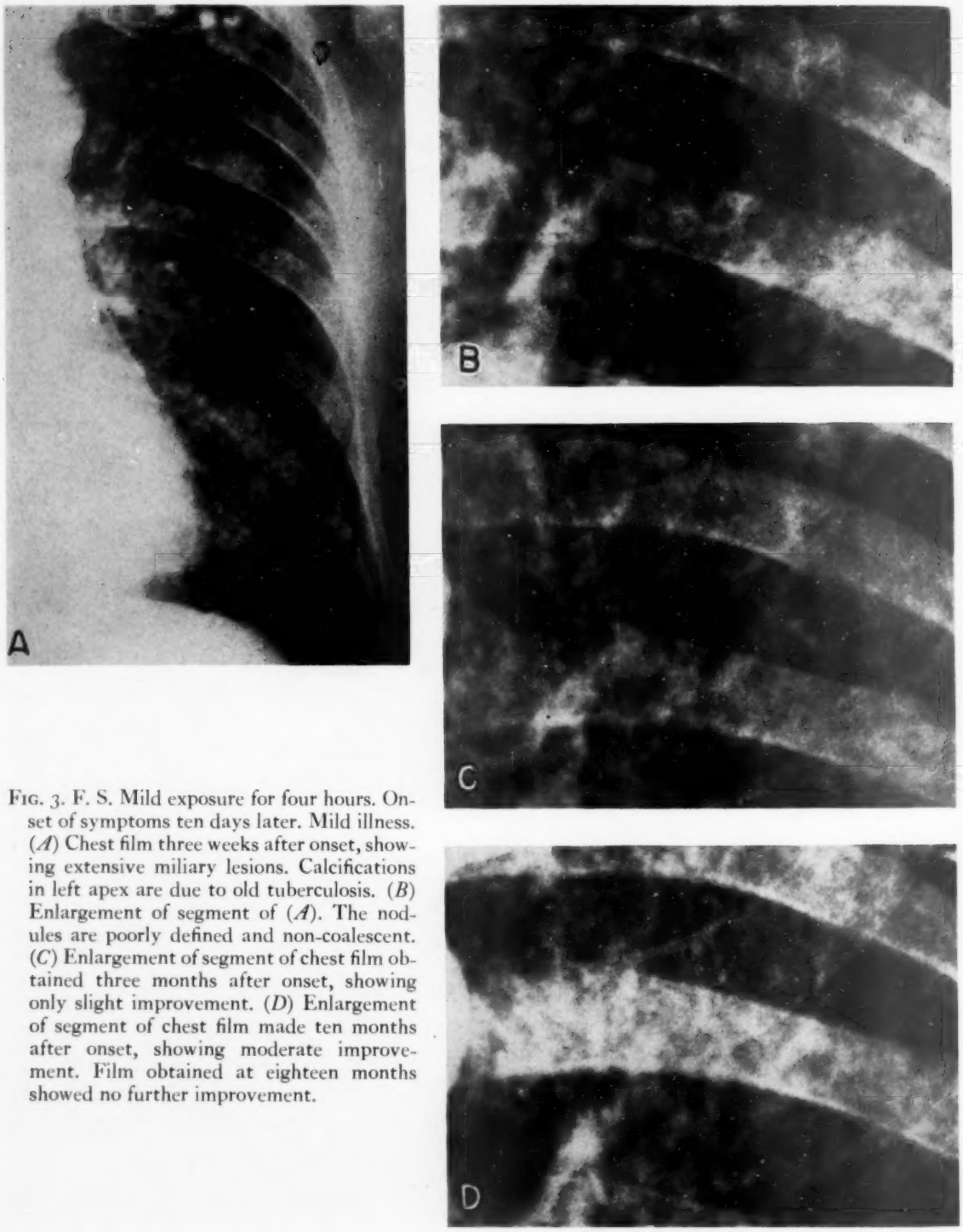

FIG. 3. F. S. Mild exposure for four hours. Onset of symptoms ten days later. Mild illness. (*A*) Chest film three weeks after onset, showing extensive miliary lesions. Calcifications in left apex are due to old tuberculosis. (*B*) Enlargement of segment of (*A*). The nodules are poorly defined and non-coalescent. (*C*) Enlargement of segment of chest film obtained three months after onset, showing only slight improvement. (*D*) Enlargement of segment of chest film made ten months after onset, showing moderate improvement. Film obtained at eighteen months showed no further improvement.

semble those of the present series. In some cases the roentgen changes persisted throughout the follow-up period of nearly six months. All patients made a complete clinical recovery. Laboratory studies were uninformative and no evidence to support the diagnosis of primary atypical pneumonia was offered.

Cain and his co-workers[2,2a,3a] reported 26 cases of an unusual pulmonary disease which occurred among soldiers in a military camp in Oklahoma in 1943. All the patients gave a history of having spent varying periods of time in a dry, abandoned storm cellar. Symptoms included malaise, chills, fever, cough and marked weight loss. Roentgenograms of the chest were said to show numerous infiltrations throughout both lung fields, varying from 1 to 20 mm. in diameter, associated with enlarged hilar nodes. The pulmonary changes gradually cleared over a period of six months. A fine diffuse pulmonary fibrosis persisted.

In 1948, Washburn and co-workers[17] described an epidemic of what they termed "cave sickness" involving 21 males who had visited an old abandoned chalk mine in southwestern Arkansas. Acute symptoms appeared in from four to thirteen days after exposure and were similar to those of the Oklahoma epidemic. Roentgenograms of the chest revealed disseminated miliary densities without evidence of lymph node or pleural involvement. Roentgenograms made ten weeks after onset showed complete clearing of the lungs in only 1 patient. In spite of extensive investigation, the cause of the epidemic was not discovered.

The roentgen findings described in these three reports resemble those which were encountered in the present study, although it should be noted that the Missouri and Oklahoma epidemics were associated with hilar enlargement, while the Arkansas and Cincinnati outbreaks were not. The similarity of roentgen changes and the similarity of exposure, symptoms and laboratory findings suggest the possibility that all four outbreaks have the same or similar causes. Further investigation will be necessary to determine if these epidemics represent a new disease entity.[5]

SUMMARY

1. The roentgenological findings observed in an unusual epidemic of an acute illness, encountered in twelve men who had been engaged in cleaning an abandoned water tower, are presented.

2. Widespread miliary lesions were demonstrable in the lungs of all twelve patients.

3. Although clinical recovery was rapid, the roentgen changes regressed slowly. In four of the twelve cases minimal pulmonary involvement was still detectable from fourteen to eighteen months after onset.*

4. The cause of the epidemic was not established.

5. Reports of three similar epidemics were encountered in a review of the literature.

We are indebted to Dr. Harry A. Feldman, Dr. Albert B. Sabin and Dr. Edward A. Gall for their assistance in this study.

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* In August, 1950, approximately three years after onset, roentgenograms showed no further change in the appearance of the residual pulmonary lesions.

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DISCUSSION

DR. ALBERT B. SABIN, Cincinnati, Ohio. The purpose of this discussion is to present some additional observations on the epidemiological, clinical, etiological and pathological aspects of the disease whose roentgenological aspects have just been presented by Dr. Felson and his associates.

The most important point in the epidemiology of this disease is that all of the men who visited the abandoned tower containing predominantly pigeon excreta developed the illness, even though the exposure of some of these men was only for a matter of ten to twenty minutes. The material in the tower was moist, and there was no evidence that the etiological agent might have been aspirated. The suggestion rather is that infection occurred by contamination of the hands with, of course, the possibility of subsequent introduction of the material into the mouth. It is of the greatest importance that no secondary cases of the disease occurred in the families of these individuals.

Clinically, the disease was of moderate to great severity in 9 of the 12 patients, and 3 had negligible signs, although you will recall that all of the patients presented the distinctive changes in the roentgenograms of the chest. Fever, headache and malaise were present in almost all of the patients. Ten of the 12 patients had a cough, but it was non-productive of sputum in almost all of them. Large doses of penicillin did not modify the course of the disease. Tests for the following etiological agents yielded negative results: ornithosis, Q fever, histoplasmosis, coccidioidomycosis, blastomycosis, toxoplasmosis, avian tuberculosis and, more recently, tests were made for Newcastle disease virus of fowls with negative results.

The death of one of these patients, as a result of an acute, myocardial infarction in an arteriosclerotic heart five months after onset of the pulmonary illness and two months after the roentgen findings in his chest were minimal or negligible, provided an opportunity to observe the pathological changes in the lungs, which were most probably the end result of his earlier illness. Multiple lesions, usually 1 to 2 mm. in diameter, were found in the lungs and peribronchial lymph nodes. The lesions were in various stages of organization but in both the lungs and the lymph nodes, there were many with central, caseous necrosis and "Langhans type" giant cells unassociated with acid-fast bacilli.

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PULMONARY CALCIFICATION—TUBERCULOSIS?, HISTOPLASMOSIS?*

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THE title of this paper is to be read complete with punctuation marks: Pulmonary calcification, dash; Tuberculosis, question mark, comma; Histoplasmosis, question mark. It corresponds to a classification in our departmental diagnosis file which is second only to "normal chest" in number of entries. This classification reflects the limitations of roentgen diagnosis with respect to etiology. In New York City, there is better than a 90 per cent chance of being right in ascribing roentgenographically demonstrable intrathoracic calcification in natives to tuberculous infection. Here in Cincinnati, the chances are roughly 3 to 1 that such an assumption would be wrong. The common occurrence, in this geographic region, of a second disease which may result in intrathoracic calcification is responsible for the loss of statistical support for our diagnostic acumen. The second disease is histoplasmosis.

Histoplasma capsulatum

Histoplasmosis was first described in 1906 by Darling,[16] who recognized it as a new disease, but who believed that the *Leishmania*-like organisms which he found in the tissues of 3 patients were a form of protozoa. He therefore gave the organism the name *Histoplasma capsulatum*. Subsequent investigators noted cultural characteristics related to certain fungi and questioned this classification. It was not until 1934 that DeMonbreun[17] conclusively identified the organism as a fungus. The fungus occurs in two forms: a yeast-like form which is the pathogenic phase, and in which it is generally found in infected tissues; and a mycelial or filamentous form in which it is much more readily cultured, and which is presumed to be the form found in nature. Experimentally, the organism can be cultivated in both phases.[17,37]

The yeast form occurs as round or ovoid cells approximately 3 microns in long axis, both free and intracellularly (Fig. 1). When stained with Giemsa or Wright stains, a basophilic mass is observed within the cell, usually eccentrically located. Sometimes a crescentic pattern is noted. A clear refractile capsule surrounds the organism in unstained specimens, accounting for the descriptive name. The yeast form is grown on sealed blood agar slants at 37° C., and can be maintained if subcultures are made frequently (three to five day intervals). If subcultures are not made, or if cultures are made aerobically at room temperature, the mycelial form develops. It is probable that the humidity maintained by sealing the slant is more important than the relative anaerobiosis in the successful cultivation of the yeast phase. Serial studies of yeast form subcultures show budding to take place at the pointed end opposite the basophilic mass. Transformation into the mycelial form occurs when buds remain attached to the parent cell and rapidly elongate to typical mycelia.

The mycelial form grossly demonstrates long filaments extending out from the massed colony. Attached to these are rounded spore forms up to 10 microns in diameter. Initially, the spores may be smooth; with the passage of time or after drying, characteristic tubercles project from the surface and produce an appearance which has been likened to an ancient Teutonic war club. The spores are relatively resistant to drying and heat. Single spores have been studied after subculture; tubercles are observed to enlarge and elon-

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gate and to develop into mycelia. These, in turn, give rise to more spores. Transformation into the yeast form occurs after inoculation of yeast free mycelia into susceptible animals[17] or by subculturing the mycelia on special media at 37° C.[6]

Since penicillin and streptomycin have no appreciable effect on pathogenic fungi (except for *Actinomyces*), the addition of at least 20 units of each per cubic milliliter of medium inhibits the growth of bacteria

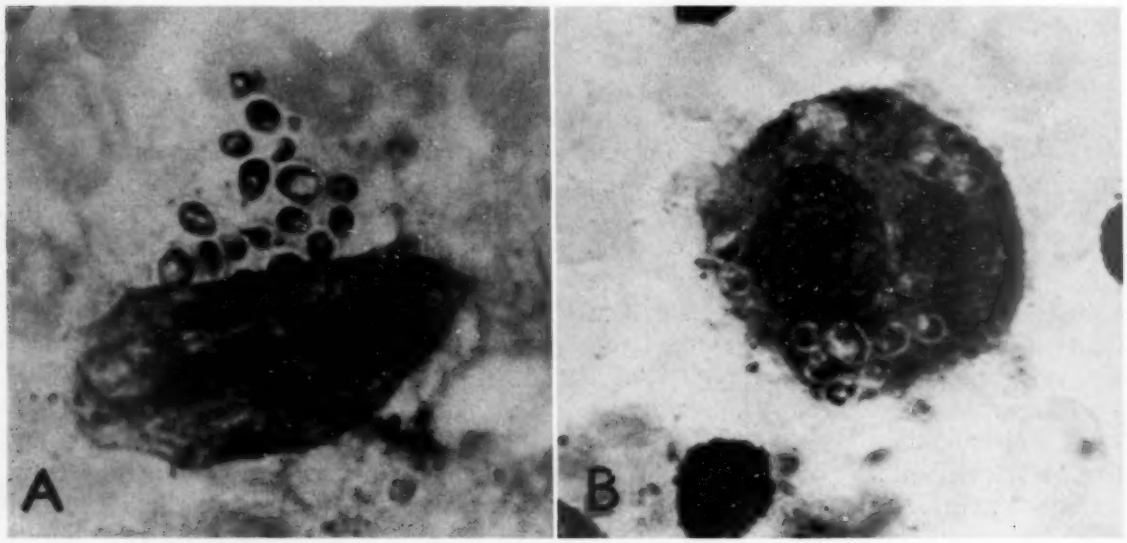

FIG. 1. (*A*) and (*B*) Extracellular and intracellular *Histoplasma capsulatum* from direct smear of bone marrow in fatal case.

which, present as a contaminant or secondary invader, might overgrow the fungus. It is hoped that further study of nutritional requirements of the fungus may result in improvement of cultural techniques.

The source of human infection has not been demonstrated. Interpersonal infection, though not impossible, would seem relatively unimportant according to studies of incidence of infection in siblings.[25] *Histoplasma capsulatum* has been found occurring naturally in dogs, rats, mice, ferrets, horses,[21,22,29] and recently in the skunk.[24] In cattle, histoplasmin skin testing has shown sensitivity with an age distribution which parallels that of humans.[29] It has been suggested from this that animals may become infected in the same manner as humans. Recently Emmons[24] has isolated *Histoplasma capsulatum* from soil in an area where naturally infected rats have been discovered. It still remains to be seen whether the animals are infected from spore-containing soil or whether the soil is contaminated by infected animals. Both possibilities may play a part in the transmission and perpetuation of the disease. The observation does seem to indicate, as Emmons points out, that *Histoplasma* has an independent saprophytic existence in nature. A saprophytic life cycle has been observed in soil inoculated experimentally. No reports of avian infection have been found. The possibility of insect vectors, too, will merit careful study.

HISTORICAL REVIEW

The history of the disease and its impact on roentgen diagnosis is a recent one. It has been recognized for the past twenty years that many individuals with roentgenographically demonstrable intrathoracic calcification do not react to tuberculin. Attempts were made to explain this apparent inconsistency with accepted teachings on several grounds. Some suggested the possibility of reversal or loss of tuber-

culin sensitivity. It is common knowledge that certain infections (particularly measles), extreme debility, and overwhelming tuberculous infection may suppress tuberculin sensitivity in known positive reactors. Dahlstrom[15] showed that over 10 per cent of tuberculin positive individuals may revert to negative in the absence of these factors. In patients with roentgenographically recognizable lesions, however, only 0.72 per cent were observed to change from positive to negative during periods of observation as long as fifteen years. Moreover, when reversals did take place in the group studied, they were observed primarily in children; adults reverted only rarely.

In certain areas of the United States, the number of individuals with intrathoracic calcification was too great to be explained by loss of tuberculin sensitivity. The value of tuberculin as a diagnostic agent was seriously questioned. For those who were firm in their belief of the specificity of the tuberculin reaction, an explanation was afforded in the suggestion that agents other than the tubercle bacillus might be responsible for intrathoracic calcification. Support for this concept followed the demonstration by Cox and Smith[11] and others[2,18] of the role of *Coccidioides immitis*, a fungus, in the production of pulmonary lesions in a sharply localized region in California. Recently, Smith *et al.*[54] revealed previously unpublished observations by Furcolow and Nelson which indicate that, as early as 1940, a fungus other than *Coccidioides immitis* was suspected as a cause of pulmonary calcification in tuberculin-negative children in Ohio. Furcolow and Nelson noted a surprising number of children reacting to coccidioidin in southwestern Ohio. This area was well out of the known endemic region for coccidioidomycosis; thus a cross reaction with other fungi became an attractive but disturbing possibility. In 1943, Smith[53] first suggested *Histoplasma capsulatum* as a possible specific agent. In a discussion of specificity of the coccidioidin skin test he stated, "Experience in testing many thousands [of soldiers] from all over the country has indicated that some individuals from Missouri, Illinois, Indiana, Michigan, Tennessee, Kentucky, Ohio, West Virginia, western Virginia, Pennsylvania, and New York may have borderline positives, while few are undoubtedly positive. This is the area of pulmonary calcifications in tuberculin negative persons and is also the endemic area of histoplasmosis."

The endemic area of histoplasmosis had been roughly mapped out in 1940 by Meleney[42] in a review of the generally fatal disease which was the only form then known. In 1943, Long and Stearns[41] mapped out the area of pulmonary calcification without reference to skin testing in a study of 53,400 chest films of inductees. They noted a high incidence of pulmonary calcifications in men from the region bounded roughly by Fort Oglethorpe, Georgia; Jefferson Barracks, Missouri; Little Rock, Arkansas; and Columbus, Ohio. A glance at their map reveals that all but two of the regions listed by Smith are included. In general, calcifications in men from this area were larger and more extensive than in men from other areas, and "miliary" spread was more common. The possibility of fungus infection was mentioned.

Other workers quickly took up Smith's suggestion. Christie and Peterson, in Tennessee, in correspondence with Smith, learned of the men from eastern central United States with positive reactions to coccidioidin on arrival in the endemic area for coccidioidomycosis in California. Reactions were much less marked than those of known infected individuals. Moreover, haplosporangin, another antigen of fungus origin, was more positive in individuals from eastern central United States than in men from the endemic area of coccidioidomycosis. Smith thought that coccidioidin and haplosporangin shared common antigens, and that another fungus probably accounted for the positive reactions to these two antigens in men from eastern central United States. Christie and Peterson then began to test Tennessee children with coccid-

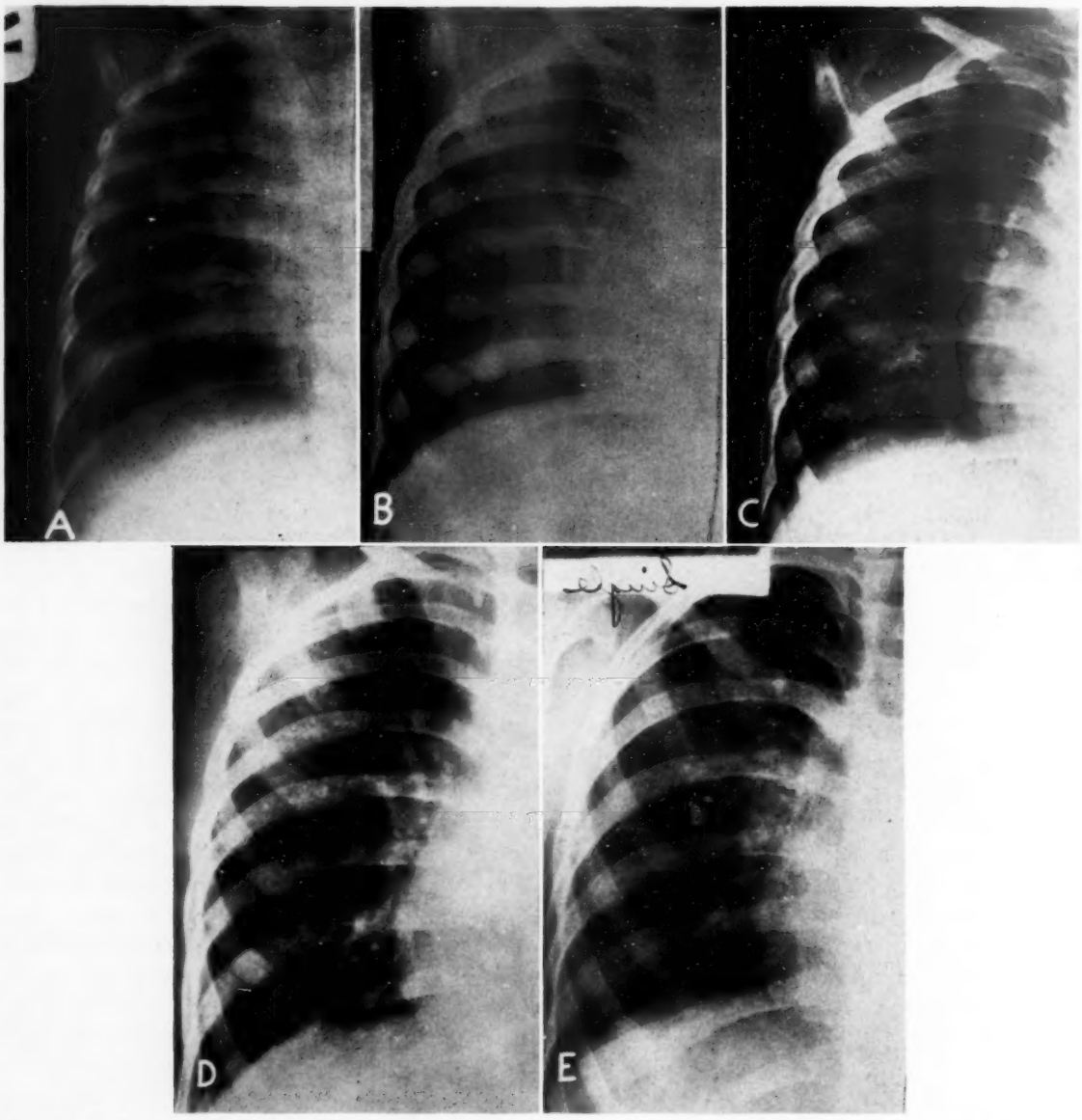

FIG. 2. Serial roentgenograms in known tuberculosis demonstrating development of calcification followed by resorption. (*A*) August 22, 1938; (*B*) September 3, 1940; (*C*) July 8, 1941; (*D*) July 14, 1942; (*E*) June 23, 1943. Roentgen evidence of earlier infection persists, but the large calcifying focus has disappeared almost completely.

ioidin but without success, and so they turned to histoplasmin. Their initial results were reported in 1945,[8] and summarized before this Society in this city in 1946. In brief, their results indicated that approximately three-fourths of the children examined showed a positive reaction to histoplasmin while about one-fourth were positive to tuberculin; 43.6 per cent showed intrathoracic calcification on roentgen examination, and 10 per cent of the individuals with calcification were negative to both antigens. The number of children positive to histoplasmin and showing pulmonary calcification was more than three times that of those with pulmonary calcification and sensitive to tuberculin. The number of individuals with positive tests and with pulmonary calcification increased rapidly in relation to age. Pulmonary calci-

fication lagged slightly behind but tended to follow very closely the incidence of positive histoplasmin tests; the curve for tuberculin reactors diverged significantly from those for pulmonary calcification and for histoplasmin reactors. In the second decade, an appreciable decrease in the incidence of calcification was observed. This suggests that resorption of calcium may take place in some individuals with histoplasmosis in a manner similar to that observed in patients with tuberculosis (Fig. 2). Another possibility is that individuals initially infected after childhood may react in a fashion which does not predispose to calcification.

At the same time (1945), Palmer[45] tested with histoplasmin and tuberculin 10,000 student nurses in sixty-five schools scattered throughout the country. The geographical localization of non-tuberculous pulmonary calcification and sensitivity to histoplasmin was almost identical to the areas outlined independently by Smith and by Long and Stearns.

Up to this time, histoplasmosis had been considered a disease of rare occurrence which was uniformly fatal. The clinical picture of the uniformly fatal disease had been clearly described by Parsons and Zarafonetis,[47] Meleney,[42] and others.[19,44] A similar study limited exclusively to infants and children was reported by Iams *et al.*[38] With experience gained in the study of coccidioidomycosis pointing the way, it seemed likely that histoplasmosis was a fatal disease in only an extremely small percentage of individuals infected. It was, therefore, a logical inference that subclinical forms of the disease exist or that mild forms which masquerade as other diseases, particularly of the respiratory system, occur; affected individuals develop a positive histoplasmin reaction and, in roughly half of them, roentgen signs of intrathoracic calcification are found. The studies undertaken in the past three years, since Christie and Peterson brought this disease to the attention of this Society, have attempted to confirm this inference and to establish the clinical nature of the so-called benign form of the disease. These studies can be divided roughly into three phases: (A) further investigation of the geographic distribution of the disease; (B) development of laboratory techniques to aid in the diagnosis; (C) attempts to elucidate the clinical nature of benign histoplasmosis.

A. GEOGRAPHIC DISTRIBUTION

On the first count, there have been many studies, local and nation-wide which have confirmed the original geographic location of the disease. Studies of school children,[8,9,10,25,26,33,35] of nurses,[32,45,46] of university students in large metropolitan universities[3,48] have all indicated that eastern central United States is, with monotonous regularity, the location for individuals with positive histoplasmin skin tests and roentgen evidence of intrathoracic calcification.

The incidence of both increases with age. Males and females are equally affected until the end of the second decade when the number of females falls off. This may reflect the influence of social factors, as marriage and domestic responsibilities may diminish the chances for exposure to new infection or re-exposure. It has not been disproved that re-infection is responsible for persistent roentgen and humeral changes. The incidence of positive histoplasmin reactors among rural residents is significantly greater than among urban residents[48] in contradistinction to the distribution of tuberculin reactors. Intra-family studies indicate that if the oldest child is positive, the incidence of positive reactions in siblings is significantly greater than if the oldest child is histoplasmin negative.[25] There is a similarity in reaction between siblings, but the similarity becomes less marked as the children grow older. It is concluded that the agent producing sensitivity is not restricted to home factors but is related to broader and less localized factors. Racial factors appear to be less important with respect to incidence than are geographic factors. The most revealing data are those pertaining to positive skin tests in individuals with pulmonary calcification. In a study[26] of over 6,000 school children in Kansas

City, Missouri, 37.6 per cent were histoplasmin positive and tuberculin negative. Approximately 16 per cent of the entire group had pulmonary calcification. Of the 828 children with pulmonary calcification, positive reactors to histoplasmin comprised 78.4 per cent. When only children with disseminated calcification were considered (62 out of 15,980), the percentage with positive histoplasmin and negative tuberculin skin tests soared to 93.5. This pattern has been repeated again and again.[8,9,10,32,35,56,63] The highest figures are obtained in studies within the geographic area of endemic histoplasmosis, but the close relationship between pulmonary calcification and histoplasmin sensitivity persists even in non-endemic areas.[1,62] Individuals with pulmonary calcification who are negative to both tuberculin and histoplasmin vary from 3 to 38 per cent. There is probably an error in both the performance and interpretation of skin tests which contributes to this discrepancy. Retests of persons with calcification show a significantly higher percentage of reaction to either tuberculin or histoplasmin than do retests of persons whose chest roentgenograms were negative.[30] Studies of small geographic units[48] have demonstrated consistent shading off of the incidence of positive reactions from regions near or in the endemic area, toward regions away from it.

B. LABORATORY PROCEDURES; SKIN TESTS

On the second count, considerable progress has been made. Techniques of culture for *Histoplasma* have been developed.[37] It has been pointed out that the organism may grow in both phases, that cultures at room temperature and incubator temperature are necessary since the organism may grow on one and not the other, and that the relatively slow growth of the culture in some cases makes necessary retention of the culture for periods of one month or longer. A carrier state, with viable fungi in the respiratory or gastrointestinal tract, has not been demonstrated, but should not be overlooked in the event of a positive culture when technical contamination can be excluded. When cultivation of an organism is difficult, a positive result is often accepted less critically than when cultivation is easy. The accessibility to contamination of the body region from which a culture is obtained should be considered in the evaluation of a positive result.[23]

The histoplasmin skin test used first in 1941 by Van Pernis, Benson and Holinger,[61] and independently by Zarafonetis and Lindberg,[64] has had extensive study. Specificity has been questioned primarily because of cross reactions with coccidioidin, haplosporangin and blastomycin.[20] Howell[36] has shown that if critical dilutions of the various antigens are used, the skin tests with the various antigens have a degree of specificity that cannot be denied. It is perhaps unfortunate that, of the many studies done throughout the country, standardization of antigens has not been possible. This probably accounts in part for discrepancies in some of the figures obtained, but makes all the more remarkable the persistently recurring results. Recently, a polysaccharide has been isolated from histoplasmin for use in skin testing.[12] The amount of material obtained is roughly 1/100 of the initial material, and its potency appears to be correspondingly increased. Some cross reaction with blastomycin was observed, but could be eliminated by serial dilution of the antigens. The homologous antigen in infected guinea pigs gave appreciably more significant results (more positive reactions) in high dilution than did the heterologous antigen. Studies are now in progress to develop the extract skin test further and include both protein and carbohydrate fractions.

Serologic tests have recently become available and are under study in several parts of the country. Two types of tests are described: complement fixation tests,[28,49,59] and agglutination tests.[50,51,52] The complement fixation tests involve standard technique; two types of antigens have been used. In one,[28,59] histoplasmin

is the antigen; in the other,[49] formalin-killed yeast-phase cells are used. Essentially similar results have been obtained in both types of tests. Infected animals demonstrate a rapid rise in complement fixing antibodies to both types of antigens shortly after infection and then a fall in titer. Uninfected animals had negative reactions, and though there is some cross reaction as with the skin test to other fungus antigens, the specificity of the complement fixation test appears to be for as long as five to six years. The yeast-phase antigen was associated with higher titers and a longer response than the histoplasmin antigen. Cross reactions with the yeast-phase antigen are not observed. The agglutination test which has been devised is a relatively simple one which involves sensitizing collodion particles with histoplasmin and exposing them to suspected serum. Nonspecific reactions occur, but strongly positive reactions have been observed only in known infected individuals

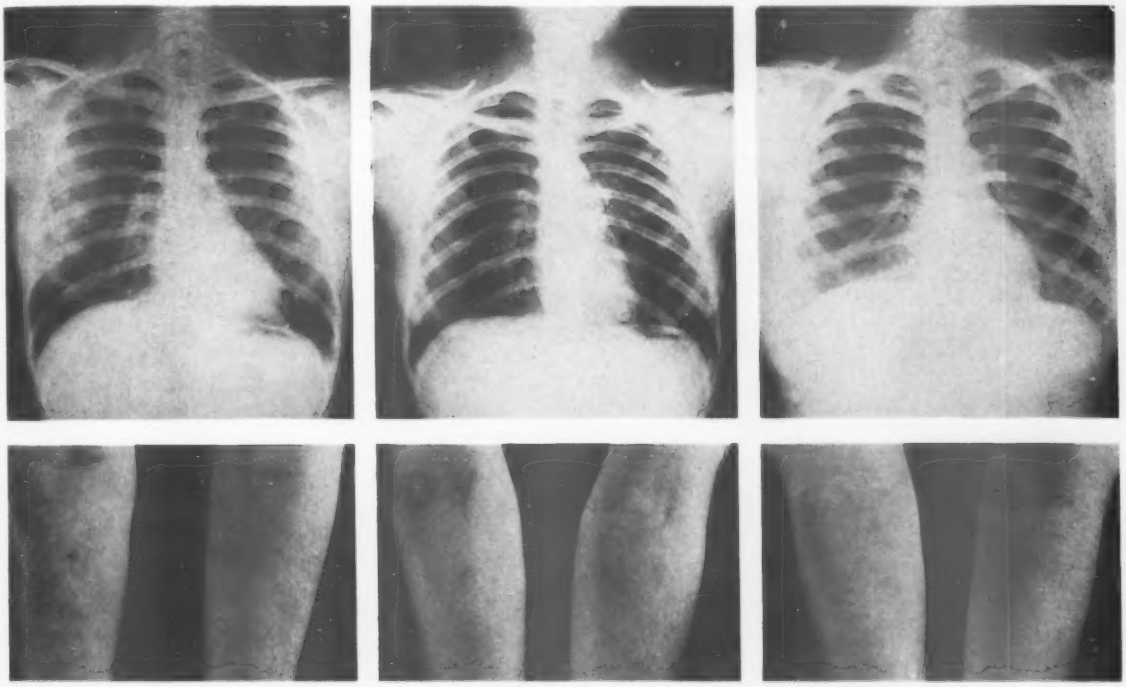

Fig. 3. Histoplasmin and tuberculin reactions and pulmonary calcification. The patient on the left has no calcification and is negative to both antigens. The patient in the middle shows a calcifying complex in the left hemithorax and is positive to both antigens. The third patient has one focus of calcification in the medial zone of the left hemithorax, is tuberculin negative and histoplasmin positive. See text for discussion.

appreciably greater than that of the skin test. This is particularly true when serial studies show changes in titer. However, further study will be necessary since variations in both complement fixation titers and skin sensitivity have been observed in proved human cases of histoplasmosis.[5] The complement fixation test, at present, is considered by some investigators[30] as an indicator of active infection. In individuals who are developing calcification in hilar lymph nodes, the test may remain positive or animals. Despite the increasing familiarity with these procedures and their interpretation, it is well to remember that they are primarily indirect and that a positive culture or direct demonstration of organisms is of tremendously greater value in establishing a diagnosis.

C. Clinical and Roentgen Features of Benign Histoplasmosis

Thirdly, reports are beginning to appear[39,58] of verified cases of "benign"

infection which tend to go on to calcification of the types seen in the geographic studies. They indicate the value of biopsy for diagnosis by culture or direct demonstration of the organisms. Diagnostic material has been obtained from bone marrow,[4,5] liver,[4] spleen,[5,19] mucous membrane ulcerations,[13,14,43] cutaneous le-

FIG. 4. Primary complex type of calcification in histoplasmosis. Histoplasmin four plus, tuberculin negative. The "mulberry" type apical focus is not diagnostic.

sions,[13,60] as well as various body fluids.[4,5,13,58] Mycologists warn against the enthusiasm which now attends the diagnosis of histoplasmosis in endemic areas.[55] The nonspecificity of roentgen findings in histoplasmosis has been stressed;[7,27] errors in roentgen diagnosis have been discussed in several recent papers[31] which indicate that etiologic diagnosis is not a strong point of roentgen examination. The indirect approach of serologic and immunologic techniques is subject to greater error in mycoses[23] than in bacterial or virus infections because of common antigenic factors in these higher forms. Fungi as yet unrecognized as pathogens may contribute to the problem of mycologic diagnosis. The problem is well illustrated by the findings in 3 technicians in our bacteriologic laboratory (Fig. 3); 2 with intrathoracic calcification, 1 without. The last is negative to PPD and histoplasmin; one with calcification reacts to histoplasmin but not to PPD, and the other is positive to both. Are the calcifications due to histoplasmosis or tuberculosis? In the one, tuberculosis is unlikely, but the positive histoplasmin reaction may be a nonspecific reaction to infection with *Coccidioides*, *Haplosporangium*, or a yet unidentified fungus. In the positive reactor to both antigens, the role of tuberculosis is likewise in doubt. Any or all of the calcifications may be tuberculous or histoplasmosal. Either disease may have been primary in the gastrointestinal system. Or, if primary in the lungs, complete healing may have taken place without roentgen sequelae, and the only evidence of infection is the tissue allergy as shown in the skin test.

An example of a typical calcifying primary complex is seen in the chest roentgenogram of one of our dietitians who has lived in Cincinnati all her life (Fig. 4). The histoplasmin skin test is positive and the tuberculin test negative. The mulberry-like primary focus has been considered by some investigators as a characteristic finding in histoplasmosis. Calcification of this type was found more frequently in association with a positive histoplasmin test than with a positive tuberculin test. However, the studies were done in areas where positive histoplasmin reactors outnumbered positive tuberculin reactors. The chances were therefore greater for any type of calcification to be associated with histoplasmin sensitivity. Roentgenologists experienced in tuberculosis have seen this type of calcification in patients with proved tuberculosis. The "halo" primary focus, likewise suspected of some specificity with respect to the diagnosis of histoplasmosis, has been discarded.[1] Fur-

colow, Mantz and Lewis[27] have illustrated variations in the roentgen picture in proved and probable cases; perhaps the only roentgen finding which alone might be interpreted as the result of histoplasma infection with any degree of probability is disseminated intrathoracic calcification (Fig. 5).

Patients with positive skin tests and intrathoracic calcification are beyond present techniques of proved diagnosis. Serial observations of proved cases strengthen the case for diagnosis in retrospect and suggest what may have happened earlier to individuals with calcification and histoplasmin sensitivity.

Zwerling and Palmer[65] have observed at least 3 nurses whose histoplasmin skin test changed from negative to positive in association with contemporaneous changes in chest roentgenograms. The clinical signs attending this change were not described.

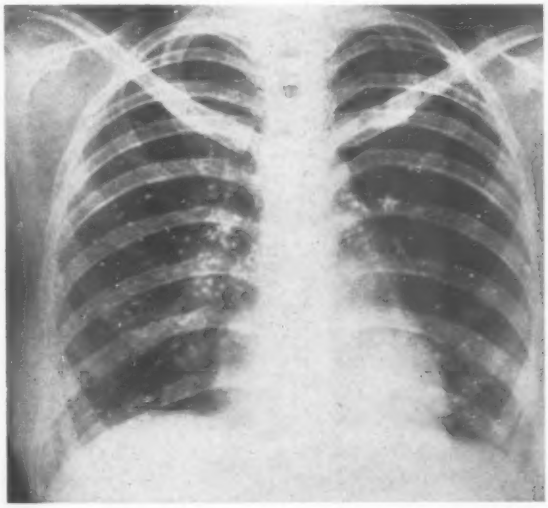

Fig. 5. Disseminated pulmonary calcification, strongly positive histoplasmin test, negative tuberculin test. Incidental chest findings in girl with hemichorea. No history of antecedent respiratory disease. Skull roentgenograms normal.

Bunnell and Furcolow[5] have reported 10 proved cases of histoplasmosis, 9 proved by culture of the organism and 1 by histologic identification. Five were alive and 5 had died at the time of the report. Two had made a complete recovery, 1 was improving

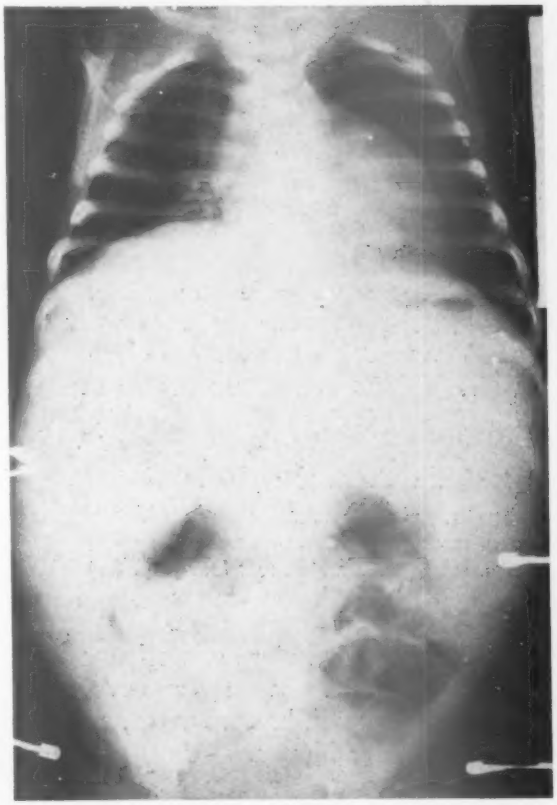

Fig. 6. Proved symptomatic non-fatal histoplasmosis. There is a suggestion of disseminated foci in the lungs, but the massive enlargement of liver and spleen is more striking.

and in 2, recovery was questionable. The disease occurred in mild and severe forms in those who lived, and did not differ appreciably clinically from early stages of those who died. The development of calcification in disseminated lesions was followed in 1 patient.

Another proved case with recovery has been reported from this hospital by Blumberg, Ruchman and Johansmann.[4] As in most of the other reported recoveries in infancy, the presenting signs were fever, pallor, anemia, hepatosplenomegaly, and cough. Roentgen examination was of interest only in indicating the enlargement of liver and spleen (Fig. 6). The histoplasmin skin test, initially negative, became positive within three months of the first examination. Skin testing with other antigens gave negative results. Comple-

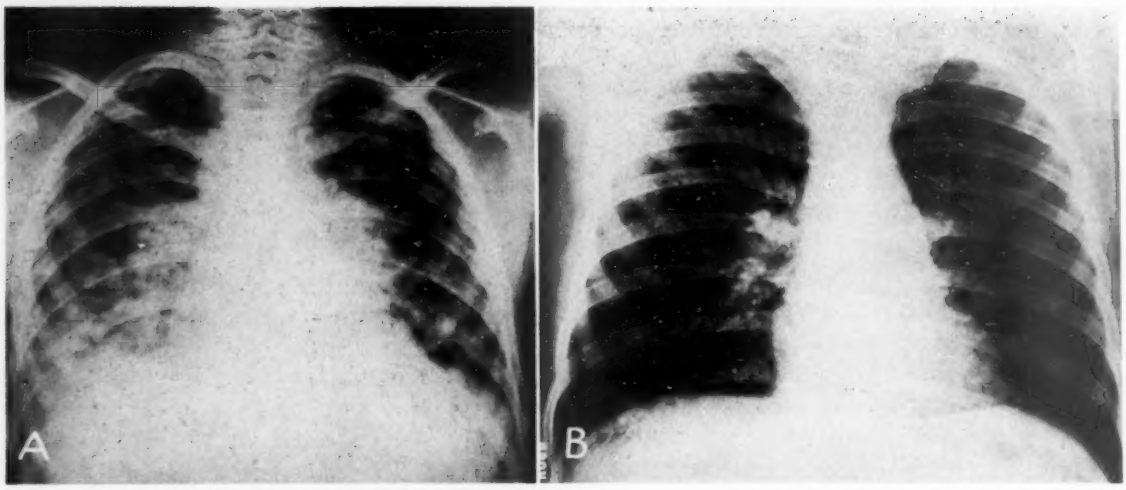

Fig. 7. Proved symptomatic non-fatal histoplasmosis (courtesy of Dr. Warren E. Wheeler). Boy, aged eight. Acute respiratory infection not responding to antibiotics. *Histoplasma capsulatum* grown from blood culture. Histoplasmin skin test four plus. (*A*) August 17, 1948, after nine days of symptoms; (*B*) December 20, 1948.

ment fixation tests were strongly positive for histoplasmosis. Diagnosis was confirmed by culture of blood, bone marrow, and material from liver biopsy.

I am indebted to Dr. Warren E. Wheeler of Columbus, Ohio, for the opportunity to include 2 more proved cases which are being reported elsewhere.[63] These are of particular interest because they occurred in cousins who are neighbors, and followed the same clinical course of fever and respiratory symptoms. The roentgen examination of the chest in both (Fig. 7 and 8) showed only a disseminated inflammatory reaction which persisted after clinical recovery. Diagnosis was proved by culture.

Within the past three months, we have recognized 2 other probable cases and proved a third in Cincinnati, primarily because we have become alerted to consider the diagnosis in all fevers of undetermined origin, particularly when associated with atypical pneumonia. Both patients with unproved histoplasmosis presented a clini-

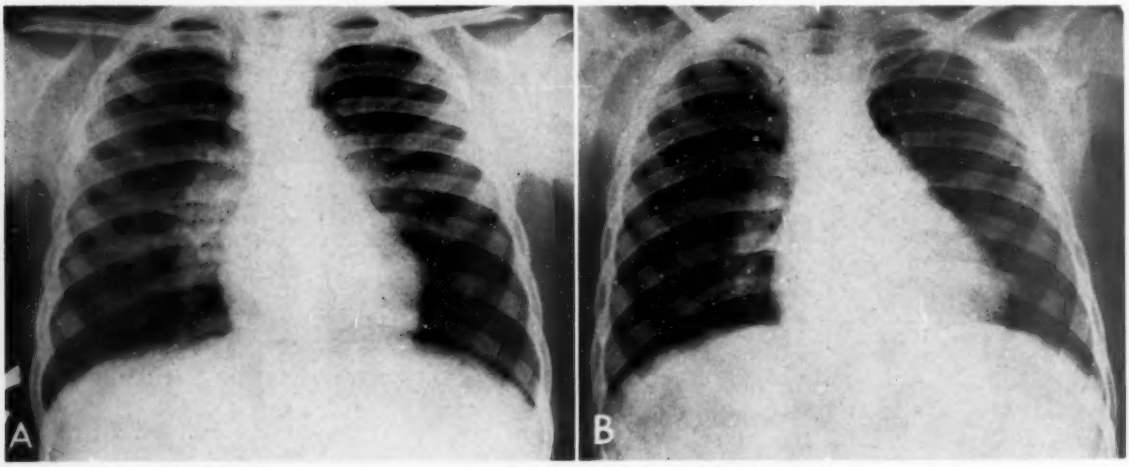

Fig. 8. Proved symptomatic non-fatal histoplasmosis (courtesy of Dr. Warren E. Wheeler). Cousin and neighbor of patient in Figure 7. Clinical course similar but onset was four days later. Histoplasmin skin test four plus. Positive blood culture. (*A*) August 18, 1948, after five days of symptoms; (*B*) February 24, 1949.

cal picture of respiratory infection with roentgen changes out of proportion to the clinical findings. Both showed disseminated inflammatory changes, 1 with massive enlargement of hilar lymph nodes (Fig. 9). The organism was not obtained from either but complement fixation tests show titers of a degree found previously only in proved active histoplasmosis.*

A review of records of the Children's Hospital discovered 7 other proved cases, 6 fatal, which differ in no respects clinically from those reported in the literature. Several other records were found of children who probably had the disease but recovered. They are presented here because they may help define the clinical manifestations of benign histoplasmosis.

Case 1. K. I., white male, aged ten. Family and past history are non-contributory. He was first admitted to Children's Hospital on November 19, 1947. Two weeks before admission, he became ill with fever going to 103° F. Cough at night soon developed. The child complained of fatigue in the late afternoon. Headache was occasionally present. He was not confined to bed prior to admission.

The positive physical findings on admission were limited to palpable cervical, axillary, and inguinal nodes. The lungs were clear to examination. PPD and histoplasmin skin tests were negative. The white blood cell count varied between 7,800 and 10,000 per cu. mm., with a slight shift to the left; 50 per cent of the white blood cells were lymphocytes. The red blood cells numbered 4.87 million; 12 gm. of hemoglobin. Erythrocyte sedimentation rate 27 mm. per hour corrected (Wintrobe). Blood culture was negative.

The fever continued but gradually fell to normal. The disease was considered a primary atypical pneumonia, treatment was symptomatic, and he was discharged December 5, 1947, sixteen days after admission.

He was re-admitted June 24, 1948, transferred from the local tuberculosis hospital. He had been well since discharge in December, 1947, but in March, 1948, developed a persistent hacking cough. In April, 1948, it became

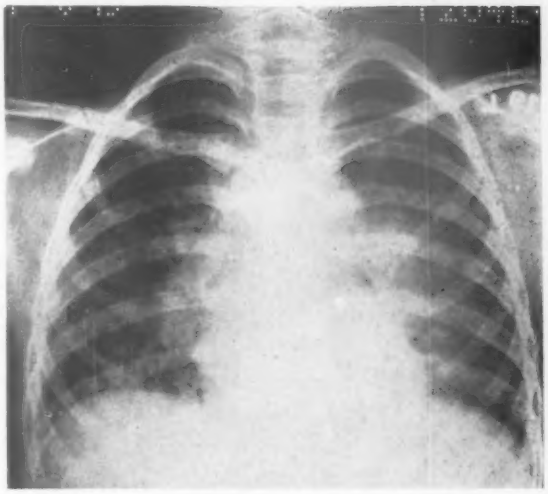

Fig. 9. Probable acute histoplasmosis. Fever of undetermined origin and respiratory infection. Complement fixation titer for histoplasmosis strongly positive. Histoplasmin skin test one plus, tuberculin test negative. Cultures negative. Clinically recovered. Roentgen findings persist.

productive of white odorless sputum. He failed to gain any weight during this five month period. In May, 1948, a routine chest film taken at a chest clinic was read as indicative of tuberculosis, probably miliary, and the boy was admitted to the tuberculosis sanatorium on May 27, 1948. At that time his tuberculin test was still negative, but his histoplasmin skin test was strongly positive. Sputum cultures and gastric lavage were negative for both tubercle bacilli and *Histoplasma capsulatum*. No clinical or laboratory evidence of illness existed at this time apart from the roentgenograms. After transfer to Children's Hospital, repeated laboratory tests, including smears and culture of the bone marrow, failed to identify a causative agent. Roentgenograms of the chest (Fig. 10), showed disseminated, fluffy, poorly defined shadows of increased density in both sides of the thorax. Hilar lymph nodes were not appreciably enlarged and no calcification was identified. The child was followed in the Out-Patient Department after discharge. He continued afebrile and was not sick. He gained weight slowly. Very little change has been observed in the chest roentgenograms for over a year, although disseminated calcification is to be expected.*

* Complement fixation tests have been done by M. L. Furcolow, Kansas City, Missouri, and Charlotte C. Campbell, Washington, D. C.

* Roentgen examination of the chest October 10, 1950, demonstrates conclusive disseminated calcification characteristic of histoplasmosis.

Comment. This patient, without tuberculosis, was placed in a tuberculous environment because of non-diagnostic roentgen findings. The error might have been avoided by proper attention to the tuberculin skin test and the clinical condition of the patient.

Case II. H. T., white male; birth date, August 18, 1943. This patient has had five admissions to the Children's Hospital. The first took place from April 27, 1944, to July 16, 1944. History obtained at that time revealed that the patient was born asphyxiated with the cord around the neck and was resuscitated with difficulty after ten minutes. A nasal discharge was noted several months before admission but this became more marked in the two months immediately preceding hospitalization. During this period the infant also had a cough associated with intermittent wheezing and rattling in his chest. There was very little fever; vomiting occurred irregularly. He was brought to the hospital because of a series of five cyanotic episodes in the preceding twenty-four hours.

On examination the infant was well developed and well nourished; he was lethargic and had a weak cry. A loose cough was present. The body temperature was 99.8° F. Small papules were scattered over the trunk and arms. "Shotty" generalized glandular enlargement was described. No rales were present although the examination of the chest indicated questionable suppression of breath sounds in the right lower hemithorax. The liver edge was palpable 2½ fingers below the costal margin; the spleen tip was 1½ fingers below the costal margin. Hypospadias was present.

Laboratory Findings. Hemoglobin varied between 8.8 and 11 gm.; red blood cell count 4.4 million; white blood cell count 11,750 with 60 per cent polymorphonuclear leukocytes on admission; later the total white blood cell count fluctuated between 7,000 and 15,000. PPD No. 1 and No. 2 were negative. Several blood cultures were sterile.

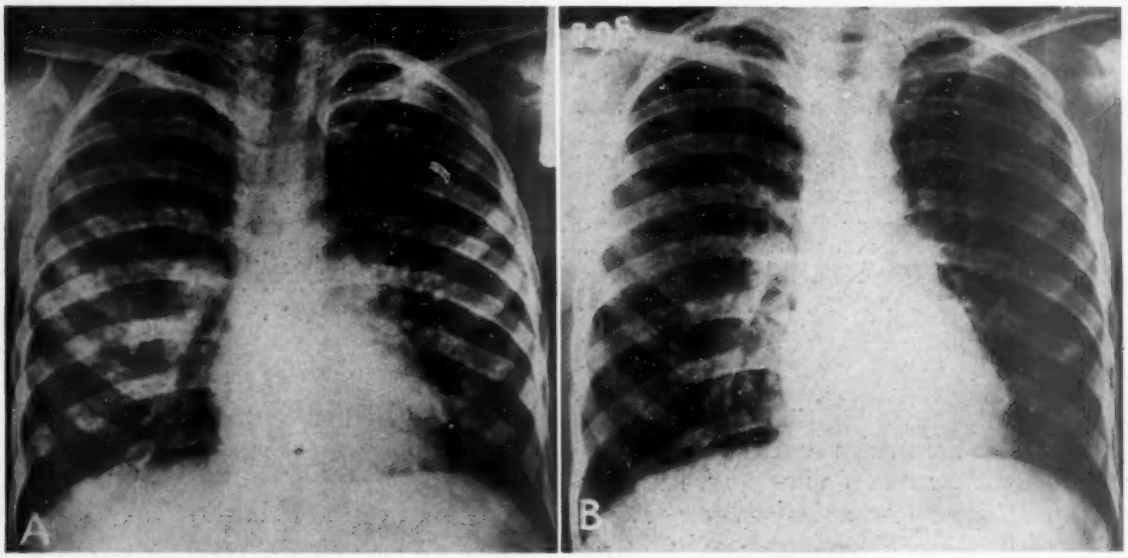

Fig. 10. Case 1. K. I., white male. Probable histoplasmosis with clinical course of atypical pneumonia. Six months later studied at tuberculosis sanatorium because of roentgen diagnosis of tuberculosis. Histoplasmin initially negative became four plus; tuberculin consistently negative. (*A*) November 28, 1947, at time of "atypical pneumonia" and negative histoplasmin. (*B*) May 11, 1949.

Treatment with sulfadiazine for ten days had no appreciable effect on the child's symptoms or signs. His temperature remained slightly elevated for nine days, and the cough persisted. Several spikes of fever occurred after sulfadiazine was discontinued, so that administration of the drug was resumed for a week. The "rattling" in the chest continued. The patient was discharged with the diagnosis of unresolved bronchopneumonia.

The second admission took place nine days later because of diarrhea, fever and vomiting. The patient still coughed. This time rhonchi were heard throughout the chest. The liver was

still palpable. He remained in the hospital for two months, but no new information was obtained. Improvement was gradual.

The third admission took place on April 16, 1945, because of persistent cough, productive and recurrent fever. Bronchograms disclosed extensive saccular bronchiectasis of the right lower lobe. On May 20, 1945, he underwent a right lower lobectomy. Convalescence was uneventful, and he was discharged on June 10, 1945. Unfortunately, there is no record of culture or histopathologic study of the removed lobe.

A fourth admission took place on October 3, 1945, because of probable bronchopneumonia. The child was discharged after two weeks.

The fifth admission, again because of respiratory system disease, was from February 18 to March 13, 1946. A histoplasmin skin test was applied for the first time and was strongly positive. PPD was still negative.

Review of roentgenograms taken during this series of admissions (Fig. 11) demonstrates that marked enlargement of the right parabronchial lymph nodes was present on September 14, 1944. By April 9, 1945, a triangular shadow had appeared in the base of the right hemithorax indicating atelectasis of the right lower lobe. The large lymph nodes, which were probably responsible for the collapse in a manner that is well recognized in primary tuberculosis, were still present. Careful inspection

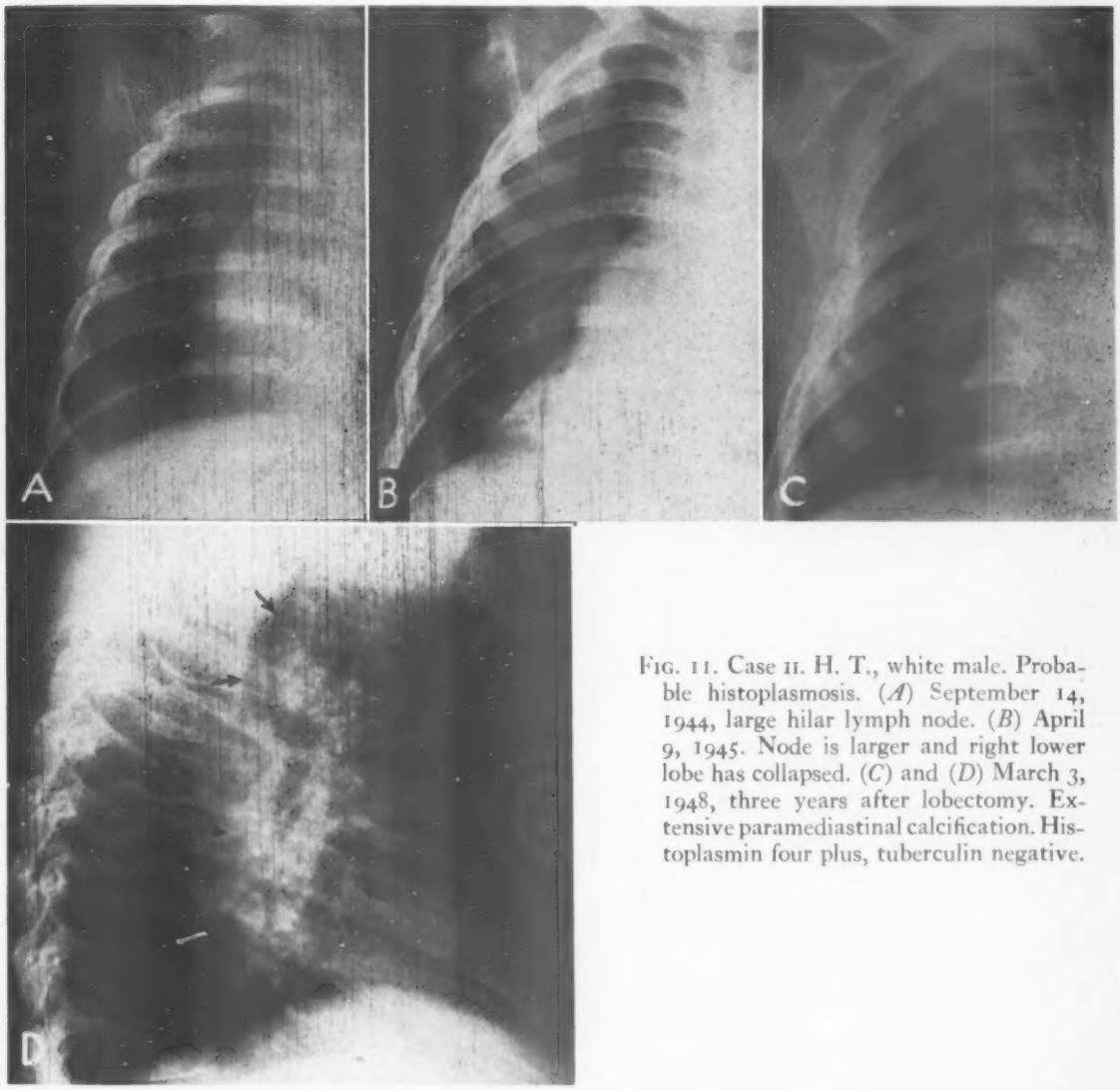

Fig. 11. Case 11. H. T., white male. Probable histoplasmosis. (*A*) September 14, 1944, large hilar lymph node. (*B*) April 9, 1945. Node is larger and right lower lobe has collapsed. (*C*) and (*D*) March 3, 1948, three years after lobectomy. Extensive paramediastinal calcification. Histoplasmin four plus, tuberculin negative.

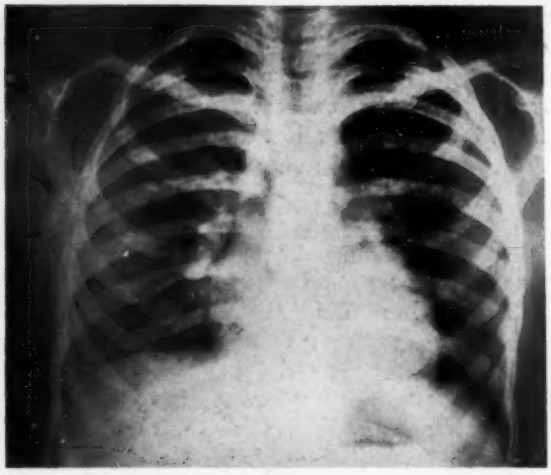

FIG. 12. Case III. S. G., white female. Probable histoplasmosis with pulmonary and extrapulmonary calcification. Histoplasmin positive, tuberculin negative. Note calcification in right axilla.

reveals that calcification is beginning to appear in the nodal shadow. Films taken three years after the lobectomy show the remaining lung to have expanded satisfactorily. Extensive calcification is now present in the paramediastinal region.

Comment. This patient probably represents histoplasmal infection which mimics another feature of primary tuberculosis—hilar lymphadenomegaly and collapse of a lobe by bronchial compression (epituberculosis). As in tuberculosis, bronchiectasis developed in the atelectatic lobe. That this sequence is not restricted to tuberculosis has been known; this patient suggests that histoplasmosis should be added to the list of conditions associated with bronchial obstruction, atelectasis, and bronchiectasis.

CASE III. S. G., white female, aged seven. This patient was admitted on March 8, 1949, because of an upper respiratory infection with fever and cough which began in December, 1948. She was treated with penicillin, but the "cold" persisted for weeks, and was accompanied by malaise, fatigability, and a low grade temperature elevation. The patient lived on a farm. She had had frequent upper respiratory infections for the preceding two years.

Her physical examination and routine laboratory studies revealed no abnormalities. PPD was negative, histoplasmin was strongly positive. Roentgen examination of the chest (Fig. 12) revealed not only intrathoracic calcification, but also calcification in a right axillary lymph node. She was asymptomatic in the hospital and was discharged after six days.

Extrapulmonary calcification has been observed frequently in tuberculosis. High[34] has reported splenic and probable hepatic calcification in histoplasmin-positive in-

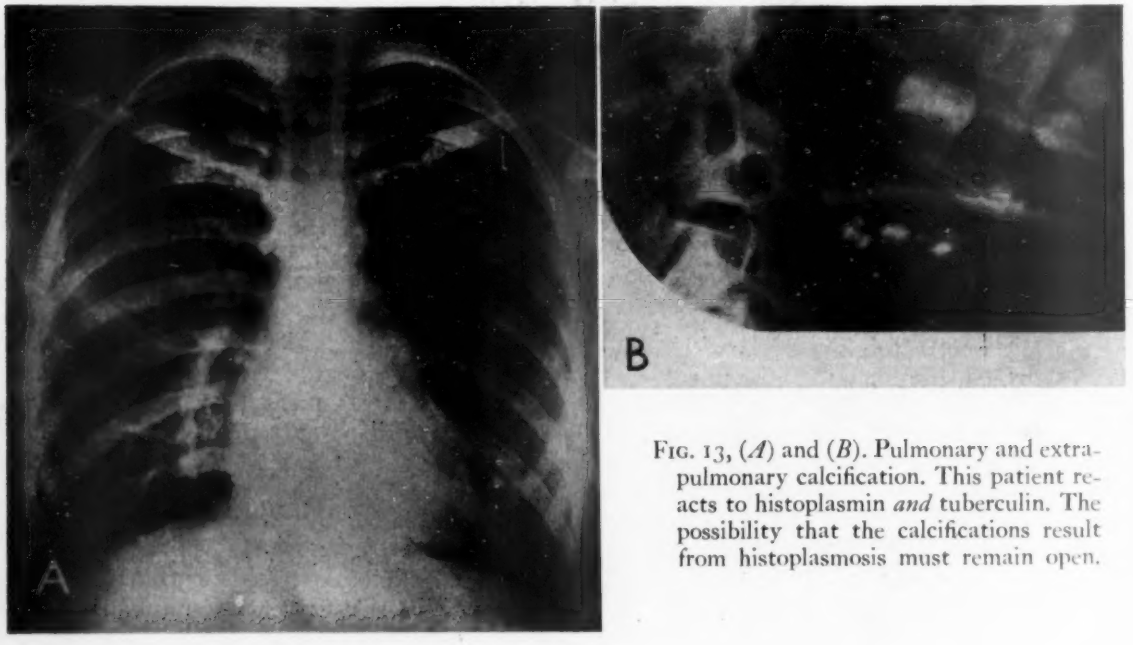

FIG. 13, (*A*) and (*B*). Pulmonary and extrapulmonary calcification. This patient reacts to histoplasmin *and* tuberculin. The possibility that the calcifications result from histoplasmosis must remain open.

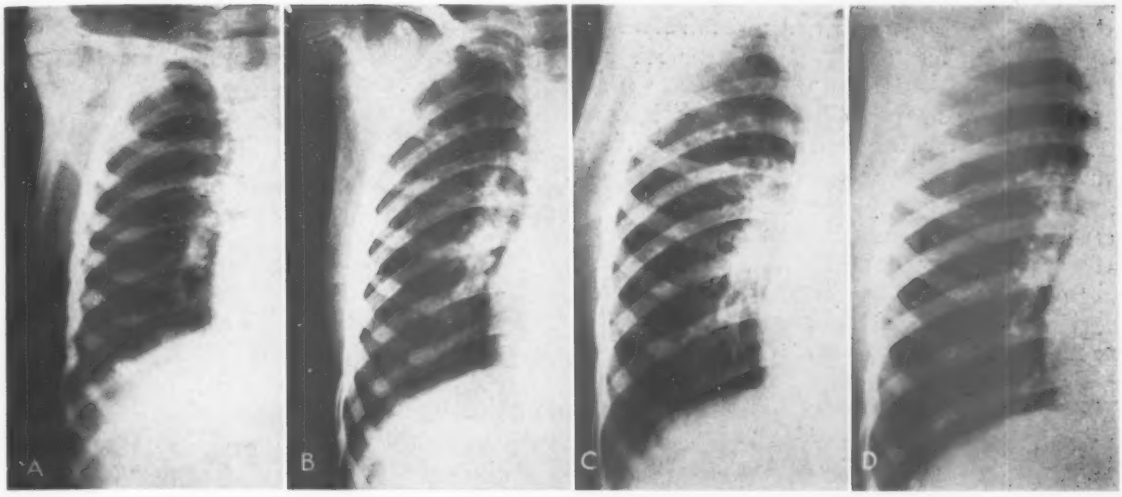

Fig. 14. Case iv. W. D., white male. Development of disseminated calcification in probable asymptomatic histoplasmosis. Histoplasmin four plus, tuberculin negative. (*A*) July 13, 1940; (*B*) May 1, 1942; (*C*) February 4, 1944; (*D*) September 11, 1945.

dividuals. It is reasonable to assume that as observations increase, other sites of calcification will be recognized. In our own experience in individuals with positive histoplasmin tests and negative tuberculin tests, we also have observed cervical lymph node calcification and 3 patients with splenic calcification (Fig. 13).

Case iv. W. D., white male, was first admitted to Children's Hospital July 3, 1940, because of malaise, fever, and pain in the hip of four days' duration. Mild diarrhea was present. Other history was non-contributory. On examination, a small right cervical lymph node was noted. The second heart sound was duplicated at the base and apex; the lungs were clear. Extensive dental caries was observed. An electrocardiogram was normal. The patient did not react to PPD; other tests, including Kahn and urinalysis, showed no abnormalities. The initial white blood cell count was 20,500 of which 79 per cent were polymorphonuclear leukocytes. Subsequent counts showed a gradual return to normal. The erythrocyte sedimentation rate was elevated. Clinical symptoms responded to bed rest and salicylates, and the patient was discharged after three weeks with the diagnosis of acute rheumatic fever.

He was re-admitted August 2, 1940, because of fever and migratory polyarthritis which began two days after discharge. At this time, a loud blowing systolic murmur was heard. Leukocytosis recurred; the elevated erythrocyte sedimentation rate persisted. Again the child responded dramatically to salicylates and bed rest, and he was discharged September 24, 1940.

Thereafter, he was followed in the Out-Patient Department and had frequent chest roentgenograms for evaluation of his cardiac status. Perusal of the chart reveals that poor nutrition was noted regularly, but at no time is there a history of respiratory symptoms.

In February, 1944, a clinical recurrence of

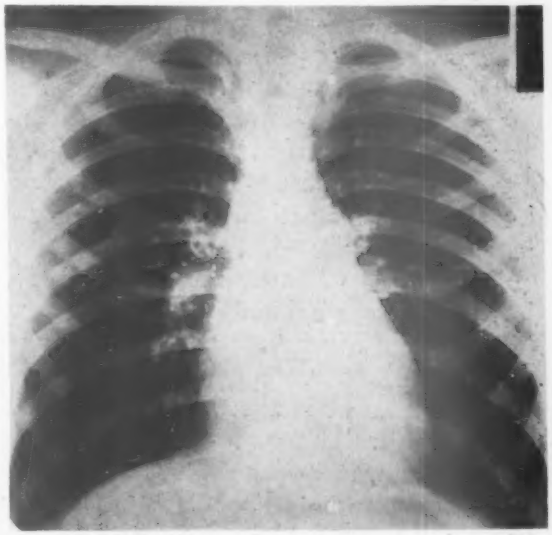

Fig. 15. Case iv. W. D., white male. September 30, 1947. Compare with Figure 5.

rheumatic fever necessitated re-admission. He had the physical signs of mitral stenosis and insufficiency.

In June, 1946, he was first tested with histoplasmin and found to be strongly positive. The tuberculin test was still negative. He was last seen in July, 1949, with inactive rheumatic carditis; his skin sensitivities are unchanged after several repeat tests.

Roentgenograms taken over a nine year period of observation (Fig. 14 and 15) reveal prominent hilar markings at the initial examination, and the gradual appearance of focal disseminated increases in density as time passed. Questionable calcification appeared in 1944 and became definite in 1945. Since 1947, all films have shown multiple disseminated foci of calcification throughout both lungs.

Comment. This child illustrates the development of disseminated calcification in the absence of clinical or roentgen signs of any acute or chronic respiratory illness. The positive histoplasmin skin test suggests that we have been privileged to observe the roentgen sequence of events in asymptomatic non-fatal histoplasmosis.

DISCUSSION

The accumulated evidence is now overwhelmingly in favor of the existence of non-fatal forms of histoplasmosis. Despite the possibility that other fungi may result in histoplasmin sensitivity, a positive skin reaction in an individual with roentgen signs of pulmonary infection who lives within the histoplasmin area places histoplasmosis high, if not first, on the list of differential diagnoses. The diagnosis is no longer made by exclusion. In this regard, it is noteworthy that *Histoplasma capsulatum* is thus far the only organism isolated from individuals with dominant histoplasmin sensitivity and focal or generalized lesions in many body systems. A big defect still remains in our knowledge of the natural history of histoplasmosis. This is the nature of the clinical manifestations of symptomatic and asymptomatic non-fatal histoplasmosis. The radiologist is in a key position to provide the missing information. By consideration of this disease when confronted with roentgen signs of pulmonary inflammatory reaction, he can stimulate the referring physicians to utilize other procedures to effect an etiologic diagnosis. As more proved cases are found and reported, the clinical picture of the disease will unfold. A new disease will be defined.

Discussion of treatment has been omitted as no conclusive data are available. Many chemotherapeutic agents have been tried but without signal effect on the progress of the disease. It may be of interest to investigate the effect of physical agents (hyperthermia) in view of the suggestive findings in experimental animal infection with other fungi.[40,57]

SUMMARY

The historical and epidemiologic features of histoplasmosis are reviewed, and recent advances in the mycology of *Histoplasma capsulatum* are described. Previously considered a rare, universally fatal disease, it is now recognized as a disease of wide distribution, generally non-fatal and often asymptomatic. Methods of diagnosis are discussed, and several unproved but probable cases are reported. The clinical nature of non-fatal histoplasmosis is still obscure. The radiologist is in a position to help clarify the problem by including histoplasmosis in the differential diagnosis of pulmonary inflammatory disease.

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GASTRIC ULCER IN CHILDHOOD

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GASTRIC ulcer in childhood is a distinct rarity. There have been only 33 cases reported in the literature. It is the purpose of this paper to present another case of gastric ulceration in a child eleven years of age. In defining gastric ulcer we are accepting the criteria laid down by Proctor in 1925 and later by Foshee in 1932. They included all cases of gastric ulcer occurring between the ages of two to fourteen years. They excluded the gastric ulcers of the newborn and those occurring with the exanthematous diseases.

That gastric ulcer is a rarity in childhood is further attested by the fact that Proctor could find only 1 case of gastric ulcer in childhood out of a total of 1,595 cases of gastric ulcer. This series extended over a period of twenty years at the Mayo Clinic. In Table 1 there is given a summary of the previously reported cases.

Etiology. The etiology of gastric ulcer in children remains even more obscure than that of peptic ulceration in the adult. This is particularly true because overwork, tobacco, alcohol and psychic disturbance cannot be considered as a cause of peptic ulceration in children. There have been no studies made of the gastric acidity in children suffering from gastric ulcer.

Sex plays no part in gastric ulcer in childhood. This was first proven by Theile in 1919. In an analysis of peptic ulceration in childhood, he showed the incidence to be 44 per cent male and 56 per cent female. These results coincide with those of Saltzstein *et al.* whose statistical analysis showed a one to one ratio between the sexes in peptic ulceration in childhood.

Pathology. It is surprising that the pathological changes should be so marked in these cases. The ulcer crater is usually very large—often penetrating. Perforation occurs in a large number of cases, having occurred in 13 of the cases of the series reported by Foshee. There is a marked predeliction for the ulcers to occur along the lesser curvature and in the pyloric portion of the stomach. The essential microscopic pathology is in no way different from that of the adult.

Diagnosis. The lack of classical symptomatology in gastric ulcer of childhood explains why it is so seldom diagnosed. The presenting symptom may be vague distress in the periumbilical region. There is usually no clear cut epigastric pain as is seen in the adult. Relief of this distress by food or alkali is seldom found in these young patients. Most commonly the disease presents itself in an ominous fashion as a complication, such as hemorrhage or perforation. Obstruction is the least common of the complications.

The difficulty in diagnosis of this condition lies in the fact that, because of its rarity, it is seldom considered as a cause of the presenting symptoms. By careful roentgen study, gastric ulcer in children can be found by the same technique as is used in adults. Gastrointestinal bleeding in children should call for a careful roentgen investigation of the gastrointestinal tract.

REPORT OF CASE

This was the first Vanderbilt University Hospital admission of this eleven year old Jewish male (History No. 177315) who had complained of sharp epigastric pain for thirty-six hours preceding admission. This was accompanied by vomiting of small amounts of coffee-ground material. There had been no tarry stools. The remainder of the history was non-contributory.

Physical Examination. Completely negative. There was no abdominal tenderness, spasm or masses. There was moderate obesity.

Laboratory Findings. Hemoglobin 10 grams; white blood cell count 15,000, with normal

Fig. 1. Posteroanterior roentgenogram shows definite crater (arrow) on lesser curvature measuring 2 cm. in diameter situated about 5 cm. proximal to the pylorus. (This is in region where ascending duodenum is superimposed, but these areas could be separated manually during roentgenoscopy.) The duodenal bulb appears normal.

differential count. Kahn test negative. Urinalysis negative. Stool, positive for occult blood.

Roentgen Study. Supine and upright films of the abdomen showed no free air in the peritoneal cavity. There was a small amount of small intestinal gas which was thought to be due to reflex ileus. Gastrointestinal series revealed the esophagus to be normal. The stomach was of the transverse type, and peristalsis was normal. There was a definite crater on the lesser curvature measuring about 2 cm. in diameter located 5 cm. proximal to the pylorus (Fig. 1 and 2; see arrow). This defect is seen in profile and *en face* views (Fig. 3). The duodenum and small intestinal pattern were normal. There was slight retention of barium in the stomach after six hours. The twenty-four hour film showed a non-significant distribution of the barium in the colon.

Clinical Course. The patient was placed on a Sippy regimen, and there was complete disappearance of the epigastric distress and vomiting. Patient remained symptom free for six weeks. Another roentgen study at six weeks revealed no crater, and the stomach appeared normal in every respect.

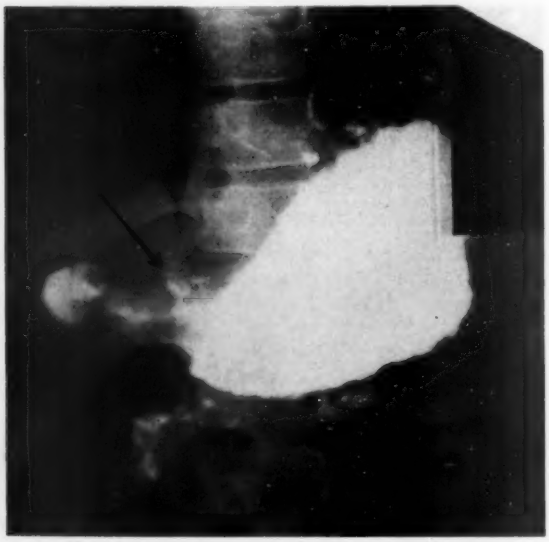

Fig. 2. Anteroposterior view shows crater (arrow) on lesser curvature previously described now remaining filled with barium as the other portions of the gastric antrum fill with air.

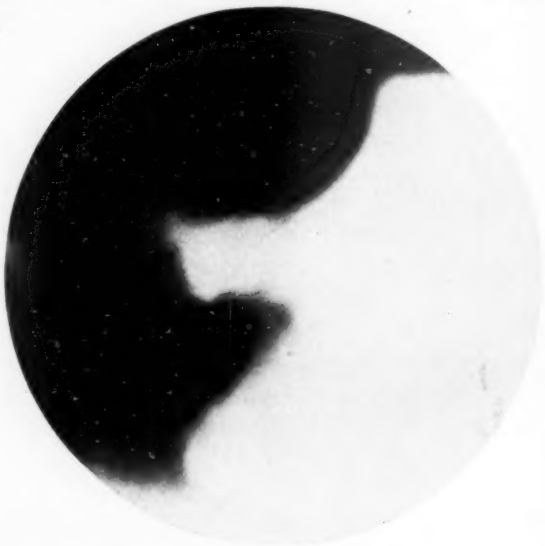

Fig. 3. Spot film with pressure shows ulcer crater *en face* (arrow) in the posterior lesser curvature of the stomach.

SUMMARY

Gastric ulcer in children is a rare occurrence. Of the thirty-three cases reported in the literature, five were found at autopsy, thirteen by surgery, and fourteen by roentgen study. Nine of the latter group were confirmed by surgery. It is interesting to note that the first four cases reported in the literature were found at autopsy, the next thirteen cases (with the

TABLE I

TABULAR REVIEW OF LITERATURE—ALL REPORTED CASES OF GASTRIC ULCER IN CHILDHOOD BETWEEN AGES OF TWO AND FOURTEEN YEARS

Author	Year	Cases	Age, Years	Sex	Site in Stomach	Method of Diagnosis
Rufz	1843	1	13	F	Lesser curvature	Autopsy
Verliac	1865	1	14	M	Posterior lesser curvature	Autopsy
Bechtold	1904	1	5	F	Greater curvature	Autopsy
Robinson	1905	1	14	M	Multiple sites—lesser curvature	Autopsy
Lund	1909	1	8	M	Anterior; antrum	Surgery
Loeber	1909	1	3	F	High; lesser curvature	Roentgen study
Cackovicz	1912	2	14	M	Pyloric antrum; lesser curvature	Surgery
			13	F	Pyloric antrum; lesser curvature	Surgery
Theile	1919	1	13	F	Anterior lesser curvature	Surgery
Sanjek	1920	1	12	F	Pyloric canal	Surgery
Carro	1922	1	8	F	Pyloric	Surgery
Norrlin	1923	1	7	F	Lesser pylorus	Surgery
Proctor	1923	1	14	M	Lesser curvature	Roentgen study, surgery
Weber	1925	1	12	M	Prepyloric; lesser curvature	Surgery
Paus	1926	2	14	M	Pyloric antrum	Surgery
			9	M	Pyloric canal posterior	Surgery
Robinson	1927	1	12	M	Anterior midwall of stomach	Surgery
Jankleson	1932	2	12	M	Lesser curvature	Roentgen study
			12	F	Prepyloric	Roentgen study
Foshee	1932	1	13	M	Posterior wall lesser curvature	Roentgen study and surgery
Olper	1933	1	11	M	Pyloric bulb	Roentgen study and surgery
Rocher	1934	1	8	M	Anterior superior wall of pylorus	Roentgen study and surgery
Micheli	1934	2	13	F	Pylorus	Roentgen study and surgery
			12	M	Pylorus	Roentgen study and surgery
Toro	1937	2	10	F	Pylorus	Surgery
			11	M	Pylorus	Roentgen study and surgery
Bertrand, Messina and Fare	1937	1	12	F	Pylorus	Roentgen study and surgery
Colson, Cade and Soustelle	1938	1	14	M	Prepylorus (rupt.)	Surgery
Burdick	1940	2	6	F	Callous lesser curvature	Autopsy
			10	F	Lesser curvature near pylorus	Roentgen study
Logan and Walters	1941	1	12	F	Lesser curvature above angulus	Roentgen study and surgery
Kraemer and Townsend	1942	1	5	M	Posterior gastric wall, pars media	Roentgen study and surgery

exception of Loeber's) were found at surgery. Of the remaining cases reported since 1932, comprising fifteen cases, all but three were initially diagnosed from the roentgenological examination.

The above tabular review (Table 1) is ample evidence of the increasing frequency with which the diagnosis of gsatric ulcer in childhood has been made with the use of roentgen examination. It points out the importance of subjecting all children with gastrointestinal symptoms, especially hem-

orrhage, to a thorough roentgen study of the gastrointestinal tract.

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END-TO-END ANASTOMOSIS OF THE COLON FOLLOWING RESECTION

A ROENTGEN STUDY OF FORTY-TWO CASES*

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INTRODUCTION

OPERABLE carcinoma of the left colon is treated by resection of the involved segment, usually with end-to-end anastomosis. After operation, roentgen examination of the colon may be requested because of abdominal symptoms to determine whether or not evidence of a recurrence of the malignant growth can be demonstrated. The barium enema often discloses a deformity of the wall at the site of the anastomosis and the question arises as to whether this is the result of the operation or of recurrence of the disease. Resection of a portion of the colon may also be done for non-malignant disease.

A search of the available literature failed to yield a report of an investigation of the roentgen appearance of these anastomoses. The purpose of this paper is to present a study of 42 cases of colonic resection with end-to-end anastomosis examined by barium enema at various intervals after the operation.

MATERIAL

Resection was performed in 36 of the 42 cases for carcinoma of the colon, in 1 case for a benign adenoma, in 2 cases for diverticulitis, in 2 cases for volvulus of the sigmoid and in 1 case for carcinoma of the ovary which had invaded the adjacent sigmoid colon.

The interval between the operation and the roentgen examination of the colon varied from a few weeks to more than seven years. Twenty-seven patients had only one and 15 had more than one examination. The great majority of the examinations were done within the first year after the operation. The technique of the anastomosis was similar in all cases. It was of the so-called "open" type. Dr. Robert S. Grinnell, of the Surgical Service of the Presbyterian Hospital, describes the technique as follows:

> The two ends of bowel to be sutured are held in Kocher clamps and brought close together. A posterior row of interrupted oooo silk mattress sutures about 4 mm. apart are placed through the serosa and muscularis. The clamps are then removed and the crushed ends of bowel opened. A continuous ooo chromic catgut suture through all layers is then started posteriorly and carried all the way around anteriorly. Finally, the anterior layer of interrupted oooo silk mattress sutures is laid.[1]

OBSERVATIONS

The contour of the colon at the site of anastomosis, as shown by the barium shadow, falls into three groups: (1) short abrupt constriction (less than 1 cm.); (2) long gradual constriction; and (3) no demonstrable deformity. In Groups 1 and 2, the narrowing of the shadow was either unilateral or bilateral. In the bilateral constrictions, the depth of the indentation on the two sides of the shadow was sometimes asymmetrical. The constrictions 1 cm. or less in length are called short and those over 1 cm. are called long. One centimeter as measured on the film was arbitrarily chosen because the majority of constrictions without local evidence of disease were about this length or less.

The short bilateral narrowing had one of two appearances. One was a constriction with abrupt, almost shelving but smooth margins through which intact mucosal folds could sometimes be traced (Fig. 1*A*).

* From the Department of Radiology, College of Physicians and Surgeons, Columbia University, and the Radiological Service of the Presbyterian Hospital, New York. Presented at the Fiftieth Annual Meeting, American Roentgen RaySociety, Cincinnati, Ohio, Oct. 4–7, 1949.

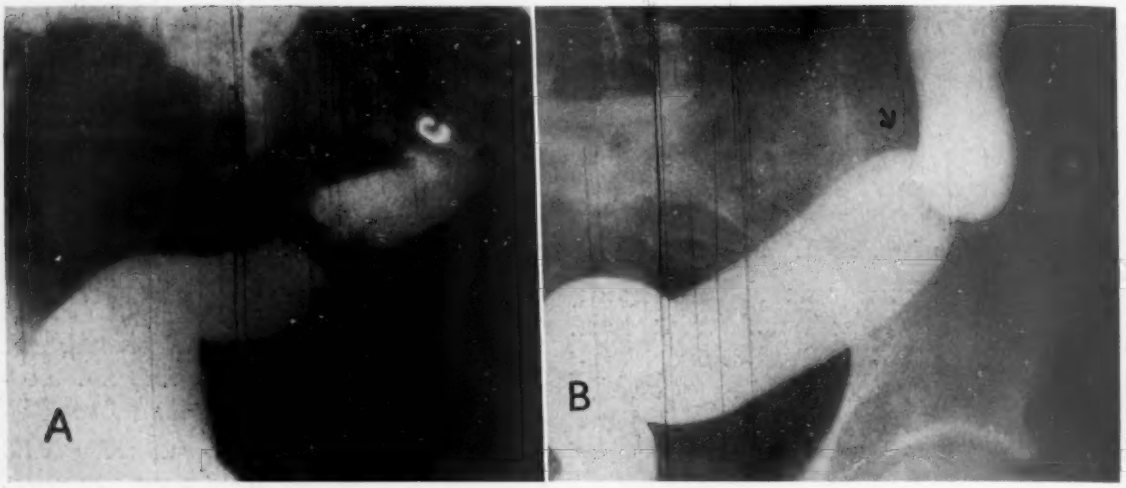

FIG. 1. (*A*) End-to-end anastomosis of the sigmoid seven months after operation showing a short bilateral constriction with smooth abrupt margins (Unit No. 828600). (*B*) End-to-end anastomosis of the sigmoid eighteen months after operation showing a short bilateral constriction with sloping margins (Unit No. 892414).

The other was a constriction which was extremely short, not more than 1 to 2 mm. in length, toward which the walls of the colon both proximally and distally sloped hour-glass fashion (Fig. 1*B*).

The long bilateral constrictions did not have the abrupt margins characteristic of most of the short bilateral narrowings. Instead there was a gradual conical narrowing from the ends to the middle of the constriction (Fig. 2).

The width of the lumen in the short constrictions was usually one-third or less of the caliber of the adjacent normal colon. The narrowing in the long constrictions was less marked and was usually more than

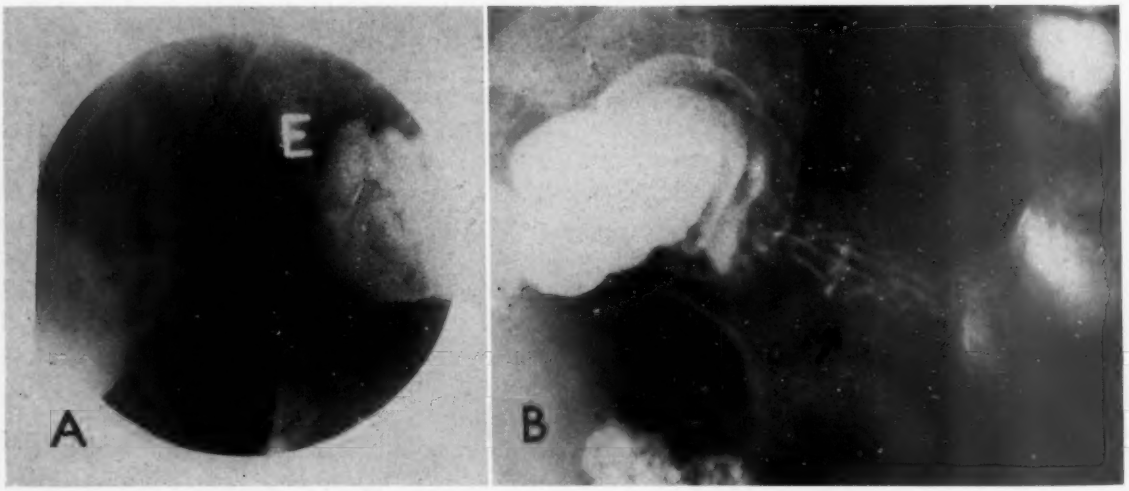

FIG. 2. Case III. (*A*) Long bilateral constriction at the site of end-to-end anastomosis (8-30-45) four months after operation, with normal mucosal folds throughout the narrowed segment. (*B*) The same constriction unchanged in length or degree of narrowing (8-6-46), almost one year after the first examination. The persistence of normal mucosal folds in the narrowed segment is shown. At this time the patient had peritoneal carcinoma metastases. This is the only one of 7 cases with long bilateral narrowing, where more than one postoperative examination was done, in which relaxation did not occur.

one-half the caliber of the adjacent normal intestine.

The unilateral constrictions will be discussed later.

DISCUSSION

At the original postoperative examination of the 42 cases, only 3 showed no abnormality at the anastomotic site. The examinations in these 3 were done eight, fourteen and twenty-three months after the operation. In the other 39 cases, a narrowing of the lumen was demonstrated which we have referred to as a constriction. Of the 39 cases, the constrictions in 27 were under 1 cm. and 12 were over 1 cm. in length as measured on the films. Of the 27 short constrictions, 26 were bilateral and only 1 (Case 1) was unilateral (Fig. 3*A*). Of the long constrictions, 9 were bilateral and 3 were unilateral (Table 1).

Of the 15 patients who had more than one barium enema after resection, subsequent examinations showed relaxation of the constriction in 10, in 1 of which (Case 1) the relaxation followed the release at a second operation of a localized adhesion at the site of anastomosis. Another (Case 11) showed a temporary increase in the length of the constriction following a biopsy through the sigmoidoscope. Of the 15, 5 showed no change in the constriction on repeated examinations.

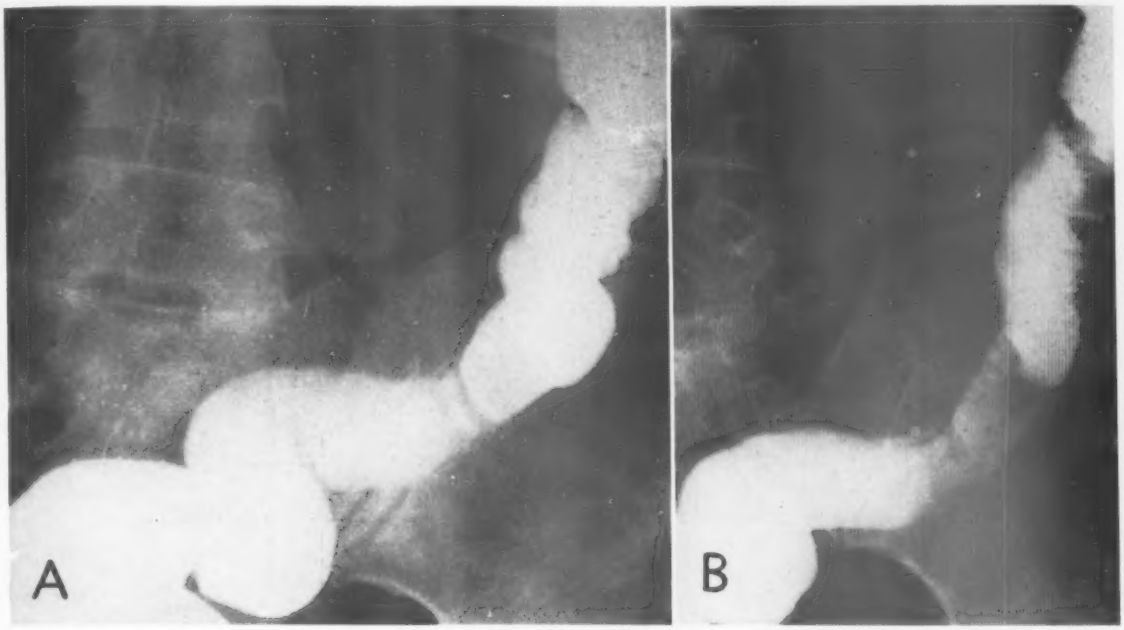

FIG. 3. Case 1. (*A*) Short unilateral constriction at the site of end-to-end anastomosis three months after resection for a carcinoma of the proximal part of the sigmoid. This is hardly more prominent than a haustrum. At the operation the omentum had been "brought down and placed over the site of the anastomosis." (*B*) Re-examination two months after that shown in (*A*) revealed an increase in the constriction. It had become bilateral and was longer. In the constriction mucosal folds can be seen on the film (arrow). This increase in the constriction in two months was interpreted by one of us (R.G.) as suggesting a local recurrence of the carcinoma, probably involving only one side of the wall and leaving the mucosa intact opposite it. At a second operation four days after this examination no evidence of carcinoma was found but an omental band was attached to the scar in the peritoneum and to the site of anastomosis. The adhesions were freed. Subsequent examinations, the last three years after resection, disclosed no defect at the site of anastomosis.

Relaxation is defined as a decrease in length or increase in the caliber of the lumen which in 4 instances resulted in complete disappearance of the constriction. Progression is defined as an increase in

FIG. 4. Long unilateral constriction at the site of end-to-end anastomosis for carcinoma of the transverse colon twenty-one months after operation (Unit No. 704126). Two weeks after this examination a second operation confirmed the presence of local recurrence of the carcinoma which on the resected specimen occupied approximately half the circumference of the colon.

length or a change from unilateral to bilateral narrowing. This occurred in only the 2 cases mentioned above and was temporary.

In Table II is shown an analysis of the changes which occurred in the 15 cases in which more than one barium enema was done after the resection. All of these 15 patients at the first examination after the operation had a constriction at the site of anastomosis, of which 8 were short and 7 were long. At the latest examination available at the time of writing, in 4 patients the constriction had disappeared and the lumen at the anastomosis was normal in width. Ten of the remaining 11 constrictions were short and only 1 was still long. The latter was associated with abdominal carcinomatosis (Case III).

Without regard to length, 35 (90 per cent) of the constrictions were bilateral. Of the 4 cases with unilateral constriction, 1 (Fig. 3) had adhesions at the site of anastomosis and 3 had recurrence of the carcinoma (Fig. 4) at the site of anastomosis. Of these 3 recurrences, 2 were proved at operation; the third had the typical roentgen picture of carcinoma of the colon and died elsewhere two months after the last barium enema and six months after the resection. The above 3 cases are the only instances of local recurrence of the carcinoma in this series.

It therefore seems that the finding of a unilateral constriction at the anastomotic

TABLE I

APPEARANCE OF ANASTOMOTIC SITE AT FIRST POSTOPERATIVE EXAMINATION

Type of Abnormality	No. of Cases	Per Cent	No. of Cases	Per Cent	No. of Cases
No abnormality	3	7			
Constriction	39	93			
Short			27	67	
Unilateral					1
Bilateral					26
Long			12	33	
Unilateral					3
Bilateral					9
TOTAL CASES	42	100			

TABLE II

ANALYSIS OF INITIAL AND FINAL APPEARANCE OF ANASTOMOTIC SITE IN CASES WITH MORE THAN ONE BARIUM ENEMA

Type of Abnormality	Number of Cases					
	Initial			Final		
No abnormality	0			4		
Constriction	15			11		
Short		8			10	
Unilateral			1			0
Bilateral			7			10
Long		7			1	
Unilateral			0			0
Bilateral			7			1
TOTAL CASES	15			15		

site must be regarded as possible evidence of localized organic disease. The fact that all 3 recurrences of carcinoma in this series produced unilateral narrowing does not preclude the possibility that other recurrences might cause bilateral constrictions.

It appears that a bilateral constriction is the usual normal and sometimes temporary result of an end-to-end colocolostomy. Two components apparently create this usual roentgenographic appearance at the site of anastomosis. These are (1) structural deformity, and (2) spasm. In any individual case either or both may be present.

The structural component is produced by the turning in of the wall by the sutures. The external layer of interrupted silk mattress sutures is known as the "inverting layer," intended to secure serosa-to-serosa contact of the two ends; this produces a narrow collar of inverted colonic wall. In some instances, this collar can be seen through the sigmoidoscope. This is undoubtedly why short bilateral constrictions usually persist; in 2 instances the constriction in the barium shadow was demonstrated as long as seventy-three and eighty-nine months after operation. The indentation in the barium shadow produced by this collar is analogous to the defect in the shadow of the barium-filled cecum produced by the inverted appendicial stump (Weber and Good,[2] 1940).

Two patients in this series were proved to have a granuloma at the site of anastomosis, each of which was attributed to the irritation of a foreign body, apparently the silk sutures, associated with low grade infection. In both, the lesion could be seen through the sigmoidoscope. It is therefore possible that some of the other short bilateral constrictions located higher up in the intestine could have been due to similar granulomas. In 1 of these 2 patients (Case IV) the constriction was so narrow that a 16F catheter would not pass through. A colorrhaphy was done and the surgical note refers to the narrowing as a "diaphragm."

That spasm plays a significant part in the production of abnormality after anastomosis is suggested by the following observations: (1) of those patients who had more than one postoperative barium enema, relaxation (Cases II and V) occurred in two-thirds; (2) tabulation of the appearance of the barium shadow with reference to time elapsed after the operation (Table III) indicates that as the time following resection lengthens, the proportion of cases showing a constriction and the number of long constrictions decrease. None of the examinations done later than twenty-four months following resection disclosed long constrictions. This suggests that the greater part of the long constriction is the result of spasm which gradually diminishes as time elapses, leaving, in the majority of cases, a short constriction which is apparently the result of the inverted collar of tissue mentioned above.

In this series, carcinoma of the colon recurred at the site of anastomosis in only 3 of 36 cases (8.3 per cent). In these, the constriction had some irregularity consistent with malignant disease. A smooth constriction with no evidence of mucosal destruction is the usual result of end-to-end anastomosis. In any individual case, statistical probabilities are of little value, and reliance must be placed on the established criteria for the diagnosis of cancer of the colon.

REPORT OF CASES

Case 1. A fifty-five year old woman (Unit No. 796298) had a resection of the sigmoid for carcinoma followed by end-to-end anastomosis August 29, 1945. The omentum was brought down and placed over the anastomosis. Three months after operation a barium enema (11–29–45) showed a short unilateral constriction at the site of anastomosis (Fig. 3*A*). A barium enema two months later (2–1–46) showed bilateral narrowing with an indentation on the lateral margin suggesting the possibility of recurrence of the carcinoma (Fig. 3*B*). At operation on 2–5–46, an omental band seemed to be compressing the site of anastomosis and was released. A barium enema four months

after the second operation (6–10–46) showed a long unilateral indentation. A barium enema eighteen months and another thirty-two months after the second operation showed gradual decrease in the deformity.

The unilateral constriction in this case was apparently due to the omental adhesion and was the only 1 of 4 cases with unilateral indentation not due to carcinoma.

Case II. A fifty-three year old woman (Unit No. 805383) had a resection with end-to-end anastomosis (11–20–45) for carcinoma at the rectosigmoidal junction. The anastomosis was the rectosigmoid junction. The mucosa was intact and the sigmoidoscopist felt that this was a cicatrix. A biopsy was taken and showed a mild inflammatory process in the lamina propria. A barium enema two days later (2–20–47) revealed an increase in the length of the constriction to 3 cm. After removal of the fistula in ano (2–25–47), the patient was well until nine months later when she noticed a few drops of bright red blood in her stool. Sigmoidoscopy on 11–12–47 again revealed a narrowing at 13 cm. through which the instrument would not pass. The mucosa was intact. A barium enema

Table III

ANALYSIS OF THE APPEARANCE OF THE BARIUM SHADOW AT THE ANASTOMOTIC SITE CORRELATED WITH THE LAPSE OF TIME AFTER RESECTION

Type of Abnormality	Number of Examinations											
	0–12 months			13–24 months			25–36 months			37–89 months		
No abnormality	1			3			2			1		
Constriction	38			15			5			4		
Short		26			12			5			4	
Unilateral			1			0			0			0
Bilateral			25			12			5			4
Long		12			3			0			0	
Unilateral			3			1			0			0
Bilateral			9			2			0			0
Total Examinations	39			18			7			5		

done with some difficulty: the surgeon had the impression that the lumen was encroached upon more than usual and was narrowed to 1.5 cm. She continued to have cramping abdominal pain and failed to gain weight. Proctoscopy (1–23–46) disclosed an ulcerating fungating mass. A biopsy was taken which showed edematous granulation tissue infiltrated with polymorphonuclear leukocytes, lymphocytes and plasma cells. Barium enema on 1-24-46, the day after the biopsy was taken, showed narrowing at the rectosigmoidal junction about 2 cm. in length. The symptoms continued and on 11–20–46 sigmoidoscopy disclosed a narrowing 13 cm. from the anus with edematous but intact mucosa. No biopsy was taken. Barium enema (12–3–46), two weeks after sigmoidoscopy, revealed a shorter narrowing, under 1 cm. in length, at the rectosigmoid junction.

Two months later, the patient was admitted for excision of a fistula in ano. Sigmoidoscopy on 2–18–47 revealed a "fixed obstruction" at two weeks later (11–26–47) showed that the narrowing had decreased in length to less than 1 cm. A barium enema on 12–27–48 and sigmoidoscopy on 1–3–49 reproduced the findings of the examinations made one year previously.

This case shows that both spasm and an organic narrowing may play a part in the constriction demonstrable by a barium enema at the site of an end-to-end anastomosis. In this case the organic factor apparently played a minor role.

Case III. A sixty year old woman (Unit No. 781269) had a resection and end-to-end anastomosis (4–23–45) for carcinoma of the sigmoid. Nearly four months later a large non-tender "grapefruit-sized" mass was felt in the right lower quadrant. A barium enema (8–30–45) revealed a long bilateral narrowing at the anastomotic site (Fig. 2*A*). On 8–31–45 an exploratory laparotomy was done and a large papillary cystadenocarcinoma of the right ovary was removed. The surgeon was able to pass two

fingers through the anastomosis in the sigmoid. The patient was well until one year later when a small mass was noted to the right of the umbilicus. A barium enema (8–6–46) again showed a long bilateral narrowing at the site of anastomosis (Fig. 2*B*) with nothing consistent with a recurrence of the carcinoma. A second exploratory operation was done 10–14–46, one and a half years after the resection, when she was found to have carcinoma metastases to the liver, omentum and abdominal parietes. No statement about the anastomosis was made in this operative report. She died two months later at home on 12–7–46.

This is the only case of the series with more than one examination in which a long bilateral constriction at the site of anastomosis did not relax. The question may be raised as to whether the peritoneal metastases played a part in this failure to relax. Unfortunately the surgeon's note did not state whether or not metastases were present at or near the site of anastomosis.

Case IV. A fifty-eight year old woman (Unit No. 898517) had a partial colectomy with end-to-end colocolostomy (2–24–48) for carcinoma of the sigmoid. The operation was not technically difficult and the anastomosis at the end of the operation was described as satisfactory. On 7–13–48, her transverse colostomy was closed. Two weeks later, she first noticed abdominal cramps. These continued intermittently for two days when it became apparent that she had developed partial large intestinal obstruction. On 8–9–48, a barium enema disclosed a constant short bilateral narrowing at the site of anastomosis (Fig. 5). Sigmoidoscopy (8–17–48) revealed at 22 cm. a diaphragm-like narrowing with an opening so small that it would not accept a 16F catheter. On 8–39–48, a colorrhaphy was done by opening the colon at the anastomotic site with a longitudinal elliptical incision through all layers and then resuturing the defect in a transverse direction. Pathologic examination of the excised piece of sigmoid wall disclosed a granuloma in which silk sutures were present. This was called a "silk granuloma," a structure which many develop when an infection occurs in tissue where silk has been used for suture material. This was the most marked constriction of the series and the only case in which a plastic operation was necessary to permit normal function at the site of anastomosis. When last seen (3–8–49), one year after the resection, the patient was free from symptoms.

Fig. 5. Case IV. Narrow short bilateral constriction six months after resection and end-to-end anastomosis for carcinoma of the sigmoid. After the transverse colostomy was closed, symptoms consistent with obstruction of the sigmoid developed. At sigmoidoscopy a 16F catheter could not be passed through this constriction. A plastic operation (colorrhaphy) was done with removal of an elliptical section from the anterior aspect of the constriction. Pathologic study disclosed a granuloma in which silk sutures were present.

Case V. On 1–20–45, a fifty year old woman (Unit No. 769311) had a resection with end-to-end anastomosis for carcinoma of the sigmoid. Upon completion, the anastomosis admitted one finger and was thought to be adequate. Postoperatively the patient complained of intermittent "griping pain" of a few minutes' duration in the right side of the abdomen. A barium enema (3–22–45), two months after resection, showed a long bilateral narrowing at the site of anastomosis with overhanging distal margins suggesting slight reverse intussusception (Fig. 6*A*) such as is often seen at the margin of a carcinoma. A second barium enema one month later (4–18–45) showed the length of the constricted segment to be less and the width of the lumen greater than at the previous examination.

At this time, the patient's complaints disappeared. About two years later, she again complained of "griping pain" in the right side of her abdomen. A barium enema (4–25–47) showed that the previously constricted segment was practically normal in caliber. A barium enema done as a check on 4–1–48 re-

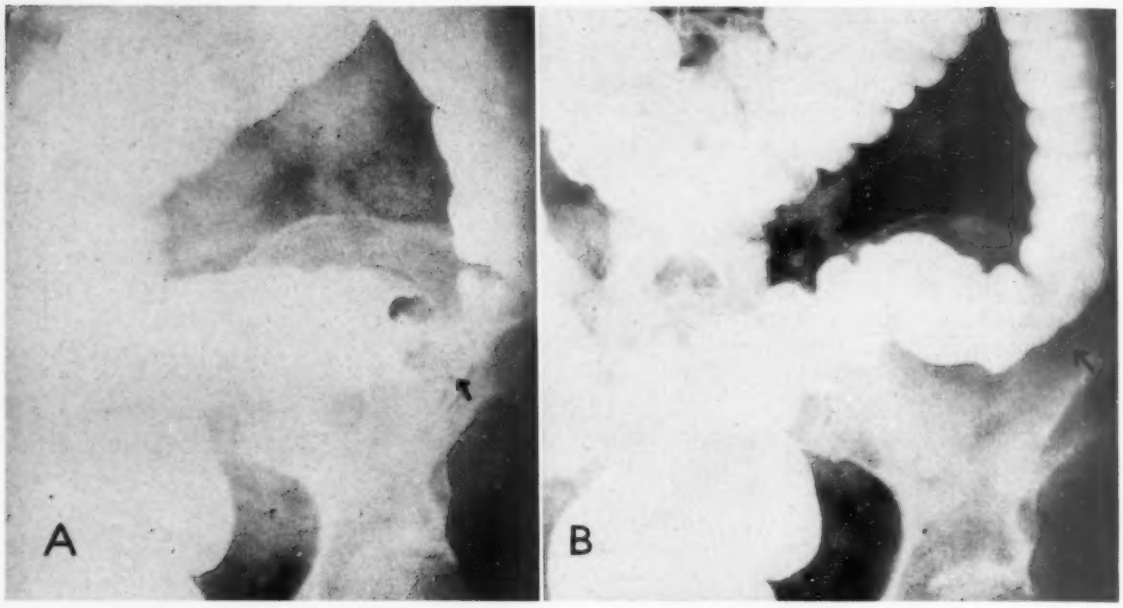

FIG. 6. Case v. (*A*) Long bilateral narrowing at the site of end-to-end anastomosis two months after operation. The contour of the distal end of the constriction simulates the appearance of well advanced carcinoma and would be so interpreted without knowledge of the resection for carcinoma two months previously. (*B*) Examination of the sigmoid three years after that of (*A*) discloses no evidence of a constriction at the site of anastomosis.

vealed no evidence of constriction at the anastomatic site (Fig. 6*B*). When last seen in the surgical follow-up clinic (7–18–49), the patient was free of symptoms.

This case illustrates the importance of spasm in producing the constriction following end-to-end anastomosis. At the first examination the contour of the distal end of the constriction simulates the appearance of a well advanced carcinoma, and would be so interpreted without knowledge that a resection had been done two months previously.

SUMMARY

1. Forty-two cases of resection of the colon with end-to-end anastomosis were studied by barium enema from a few weeks to more than seven years after the operation. Twenty-seven had only one examination; 15 had more than one. Thirty-six of these operations were done for carcinoma of the colon.

2. Thirty-nine (93 per cent) showed some abnormality at the site of anastomosis at the first examination following operation. In 3 patients no abnormality was found.

3. The abnormality was a constriction, which was less than 1 cm. in length in 27 and more than 1 cm. in 12; was bilateral in 35 and unilateral in 4.

4. A structural change in the wall resulting from the anastomosis is probably the cause of most of the short constrictions. Spasm adjacent to the anastomosis seems to play a part in the longer bilateral constrictions and in this series the spastic element diminished or disappeared with the elapse of time except in one case with abdominal carcinomatosis. One short bilateral constriction was no longer present twenty-five months after the first examination and thirty-five months after the operation.

5. Unilateral narrowing at the site of anastomosis was associated with a local recurrence of carcinoma in 3 and with a local adhesion in 1 of 4 cases.

6. This study of end-to-end anastomosis of the resected colon suggests that a short bilateral constriction will be found in the majority of cases. In the individual case, a diagnosis of local recurrence of carcinoma

must rest upon the already established criteria for carcinoma of the colon.

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DISCUSSION

Dr. James T. Case, Chicago, Illinois. This kind of a paper is an excellent addition to our consideration of post-operative colonic function. It is in keeping with our experience over a good many years and observation of postoperative cases. As is usual with the authors of the paper, the subject has been analyzed and systematized so as to make it perhaps more valuable than a routine running comment on post-operative cases.

Anastomoses have been made laterally and end-to-side and also by a gun-barrel method when the exteriorization of the tumor has been desired. However, the authors have chosen the commoner and nowadays preferred method of end-to-end anastomosis. Their observations are accurate and their conclusions highly reasonable. My own observations agree with them perfectly.

There is one type of end-to-end anastomosis which they did not mention and which permits one further observation and that is an end-to-end anastomosis done very low in the colon, really a sigmoidorectal anastomosis. In this operation the surgeon introduces a tube in the rectum before the operation is begun, and then after the anastomosis has been completed, because of the insufficient amount of serosa available for re-peritonization, the tube is passed on up into the sigmoid above the anastomosis, attached by temporary plain catgut suture to the bowel; and then with an assistant pulling down on the tube from below, the proximal end of the anastomosed colon is intussuscepted for a short distance and a further row of interrupted silk serosal stitches taken for safety.

I have done myself a few cases of that sort and I have seen a number where there was a constriction of the bowel at the anastomotic site which it was necessary to dilate by proctoscopic or sigmoidoscopic methods at intervals of several months after operation during a period of several years before the dilation became permanent.

One wonders on study of the illustrations which have been put on the screen whether the filling defect pointed out may not be due in part to a tendency to intussusception of colonic mucosa of the afferent loop towards the anastomotic site. One gains that impression, looking at some of the films. A very interesting problem arises when other types of anastomosis are investigated, especially in those cases where the terminal ileum and proximal colon have been resected and an end-to-side anastomosis has been done; what part does intussuscepted mucosa play? Our studies have impressed us with the need of making this end-to-side anastomosis the nearest possible to the blind end of the colon in such cases, so as to leave no sacculation for retention of colonic content. Otherwise, there is left a pocket which will retain the barium and the ordinary residues to a degree often sufficient to cause pain. The gun-barrel type of anastomosis also permits some interesting observations.

This is a very satisfactory paper and one of the kind we like to hear.

Dr. Sharpe (closing). I agree with Dr. Case that some of these constrictions that we see at the site of anastomosis really look as if there had been intussusception. However, I think that is true only in a few cases, but certainly not in the majority of cases. As far as the sigmoidorectal anastomosis with a catheter is concerned, we did not find any such cases. This operation was apparently not done on any of the cases at the Presbyterian Hospital.

THE PRONE POSITION IN THE ROENTGENOLOGICAL DIAGNOSIS OF FREE INTRA-ABDOMINAL GAS

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THE presence of free intra-abdominal gas is of utmost importance in the diagnosis of acute abdominal conditions, and its demonstration by roentgenological methods is a well established procedure. The recognition of free gas beneath the diaphragm usually requires the upright, lateral, or lateral decubitus projections. Since occasionally the patient is examined by necessity or through an omission only in the prone or supine positions, it is the purpose of this paper to present the roentgen findings of free intra-abdominal gas under these circumstances.

The upright position for the roentgenological diagnosis of perforated peptic ulcer was first proposed by Popper[4] in 1915. In 1925 Vaughn and Brams[7] reported accurate diagnosis of 82.2 per cent of 29 cases of perforated ulcers, and urged the use of the upright or the lateral decubitus positions for visualization of free intra-abdominal gas. In 1929 Vaughn and Singer[8] were able to obtain evidence of pneumoperitoneum in 87 per cent of 63 cases. All of the 21 cases of perforated ulcer reported by Spinzig[5] in 1933 showed free abdominal gas. The upright, as well as a lateral roentgenogram was recommended by Pendergass and Kirk[3] in 1927; they also advised caution in this diagnosis because of the possibility of a hepatoptosis. In 1938 Paine and Rigler[1] advocated the use of the left lateral decubitus position, in addition to the upright and flat views, for a more accurate diagnosis. They determined that as little as 5 to 10 cubic centimeters of free air could be demonstrated in the abdomen. By 1943 Pearce[2] had recommended the table be tilted so that the highest peritoneal pocket lay above the liver to better demonstrate a pneumoperitoneum.

ACCURACY OF DIAGNOSIS

The roentgenological diagnosis of perforated peptic ulcers is seldom 100 per cent accurate because the conditions are not always entirely satisfactory for the demonstration of free intra-abdominal gas. The patient may be large, the roentgen rays may not be vertical to the diaphragm, or the presence of intra-abdominal adhesions make the diagnosis difficult. Free gas will be absent if the perforation is located below the fluid level in a hollow viscus,[1] or there is no gas in the hollow viscus at the time of the perforation. Occasionally only the supine or prone films are possible; and when upright and lateral decubitus views are inconclusive, it is reassuring to confirm the presence or absence of a pneumoperitoneum by the visualization of small amounts of free gas in the flat films.

REVIEW OF CASES

Twenty-nine cases of perforated hollow viscus were reviewed for evidence of free intra-abdominal gas. The diagnosis of perforated viscus was established either by post-mortem examination or by surgery. Films were taken in the standard projection of upright, lateral decubitus, and supine or prone positions. A positive roentgenological diagnosis of perforated hollow viscus was made in 23, or 79.3 per cent, of the 29 cases. Of the 6 cases that were missed 3 were perforations into the lesser sac, 1 was a duodenal ulcer that had perforated into the bed of the liver, 1 was an anterior duodenal ulcer, and 1 was an anterior gastric ulcer.

Prone or supine films were available in 26 of the series, and when these were reviewed, they revealed constant findings that could be interpreted as free intra-abdominal gas

Fig. 1. Abdominal prone film showing a large collection of free gas at the outer margins of both kidneys due to a perforated gastric ulcer.

Fig. 2. Upright abdominal film of same case as Figure 1 showing a large amount of free gas beneath the diaphragm.

in 19 cases. It appears of value to note that 3 of the 19 showed signs of gas on the prone views while the upright films were interpreted as negative. In 1 case free gas was

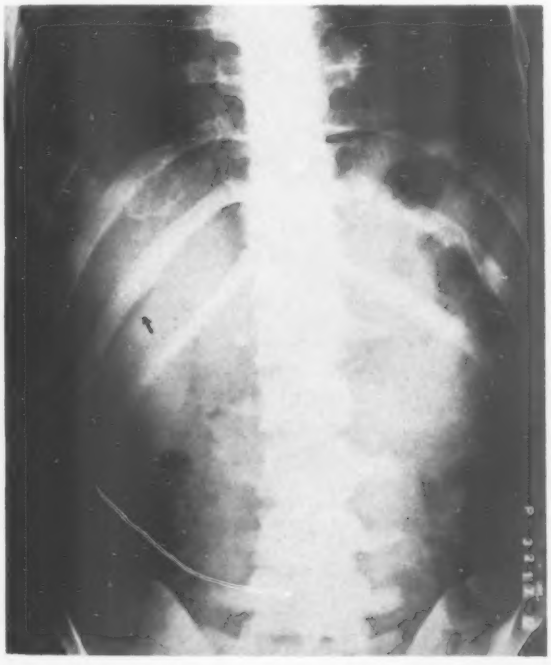

Fig. 3. Abdominal prone film showing the collection of a small amount of free gas at the outer margin of the right kidney due to a perforated duodenal ulcer.

Fig. 4. Upright abdominal film of same case as Figure 3 showing a very small amount of free gas beneath the diaphragm on the right side.

seen in the prone film twenty-four hours before it was demonstrated in the upright projection.

With free intra-abdominal gas the prone films showed an area of decreased density within the liver shadow which has for its medial border the upper pole of the right kidney. The size of this shadow depended upon the amount of free gas within the abdomen. A similar shadow could often be seen on the left side between the outer border of the kidney and the inner margin of the spleen (Fig. 1 and 3). In the supine films areas of decreased density interpreted as free abdominal gas could be seen between the liver and the diaphragm, or between the spleen and the diaphragm.

The reason for the collection of gas at such locations is attributed to these portions of the abdominal cavity being at the highest level when the patient is in the prone or supine positions. The gas seeking the highest level accumulates at these areas and can be visualized on plain roentgenograms as shadows of decreased density.

CONCLUSIONS

The rupture of a hollow viscus can be determined by the presence of free intra-abdominal gas in about 80 per cent of the cases. A negative diagnosis does not eliminate the possibility of a perforated viscus for peptic ulcers that rupture posteriorly are often missed. The diagnosis of free intra-abdominal gas can be made from the prone or supine films by the presence of an area of decreased density in the liver shadow at the outer border of the right kidney, or between the spleen and the left kidney, or the spleen and the diaphragm. These findings on a flat film warrant further investigations in the upright and lateral decubitus positions for the presence of a pneumoperitoneum.

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ROENTGENOLOGICAL DIAGNOSIS OF SPONGE IN THE ABDOMEN

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SEARCH of the literature fails to reveal any evidence that a sponge in the abdomen was ever identified on a roentgenogram without the use of specially prepared gauze impregnated with opaque material, or gauze to which metallic clips were attached for identification. The following case report is of interest chiefly because we were able to positively identify an unusual shadow as a shadow caused by a sponge in the abdomen.

The importance of this diagnosis is readily appreciated by any surgeon who has had the misfortune to reopen an abdomen and find a sponge. The present methods and devices of sponge control do not provide adequate security against the loss of a sponge. The devices that have been tried include the use of "rayable gauze"—gauze prepared with radiopaque thread[3] and gauze to which metallic rings are attached.[1] The former is not in general use, probably because of the additional expense involved and the latter is practical only with the use of a large lap pad and not for small sponges. At any rate, neither of these methods is in use today and reliance is placed solely on sponge count and extreme care. Unfortunately, however, mistakes are occasionally made.

The dire results of leaving a sponge in the abdomen have been well described by Greenhill.[2] They include pain, ileus, intra-abdominal abscesses, sinuses, bladder and rectal disturbances, adhesions and intestinal obstruction. Delayed postoperative mortality is not unusual. Any means of enabling a roentgenologist to make a diagnosis of sponge in the abdomen early in a stormy postoperative course can reduce the morbidity and mortality considerably.

CASE REPORT

H. R., aged thirty-five, a prisoner of war, came to our Army Evacuation Hospital as a transfer case from a field hospital. Three weeks before admission he had received multiple abdominal wounds from shell fragments. The fragments ruptured the peritoneum, lodged in the liver and caused multiple perforations of the small and large intestines. The perforated intestines were repaired and the liver wounds debrided and drained. When he arrived at our hospital the operation and drainage wounds

FIG. 1. Routine supine film showing enormous gastric dilatation, diagnostic of pyloric obstruction. The gas trapped in the sponge is clearly seen in the right upper quadrant.

were both healed. However, the patient was very ill and ran a stormy course. He was emaciated and suffering from chills, high fever, abdominal pain and vomiting. A roentgen examination of the abdomen was ordered. Figure 1 is a routine supine film. Figure 2 was taken with the patient lying supine, the film held vertically to one side and the central ray perpendicular to the film. These two films were our routine in all abdominal wound cases.[5] These films show the most marked gastric dilatation we have ever seen. Despite the enormous gastric dilatation there is an absence of air in the remainder of the intestinal tract, an obvious diagnosis of pyloric obstruction. In addition, there is a collection of air under the diaphragm, visible through the gas in the stomach (Fig. 2). At the base of this collection

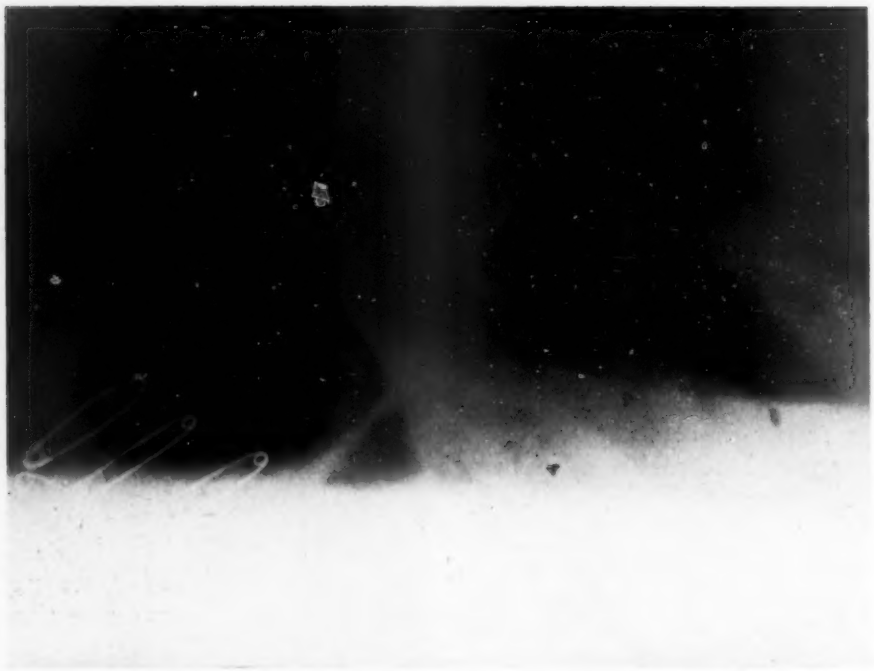

FIG. 2. Lateral recumbent view, taken with the patient lying on the back and the film held vertically to one side. This shows the enormous gastric dilatation. The collection of air close to the diaphragm is the subphrenic abscess and at the base of the abscess an arrow points to the necrotic liver. The air within the sponge is barely visible close to the gas filled duodenal bulb.

of air there is a soft tissue shadow with a markedly irregular contour. This collection of air was interpreted as a subphrenic abscess and the irregular soft tissue shadow as a necrotic liver. The following day erect films were taken to more clearly demonstrate the subphrenic abscess. Figure 3, taken in the erect position, demonstrates a large subphrenic abscess with the usual associated findings at the base of the right lung. Figure 4, taken with the patient lying on his left side, the cassette in contact with his back and the central ray horizontal and perpendicular to the cassette, shows a fluid level under the right diaphragm. Figure 5, taken in the same manner as Figure 4, except that the patient now lay on his right side, shows a fluid level in the stomach at the upper end of the film, and a fluid level in the abscess at the lower end of the film.

Thus a diagnosis of a large subphrenic abscess and complete pyloric obstruction was established. Upon reviewing the roentgenograms, a peculiar localized collection of small bubbles of air was noted in the right upper quadrant (Fig. 1). The complete absence of gas in the intestines, the localization to the right upper quadrant and the small, poorly defined bubbles made it unlikely to explain the shadow as gas in the intestinal tract. In Figure 2 the same peculiar, localized, small gas shadows may be seen in close association with the abscess cavity. There is no change in the appearance of this collection of air in different positions over a period of several days.

About three months before we had seen a case of intestinal obstruction due to a sponge

FIG. 3. Erect film of the abdomen showing large subphrenic abscess with fluid level under the right diaphragm.

Fig. 4. With the patient on his left side, the fluid level of the large subphrenic abscess is seen in the upper end of the film.

left in the abdomen. The thought occurred to us that a similar diagnosis could account for the entire clinical picture and the unusual roentgenogram. One need only imagine air trapped within the mesh of the sponge to explain the shadow of a collection of small gas bubbles that does not change in various positions or on various days. Gas in the intestine is enclosed by a limiting membrane and is more sharply defined. The presence of a pyloric obstruction

Fig. 5. With the patient on his right side, the subphrenic abscess is seen under the diaphragm in the lower end of the film.

and the absence of gas in the remainder of the intestines undoubtedly helped us in reaching this diagnosis. However, the shadow is sufficiently characteristic to be recognized, even with the presence of intestinal gas.

After having considered the diagnosis of sponge in the abdomen, it hardly seemed possible to entertain any other diagnosis. The patient was operated upon five days after admission and a small sponge was found in the right upper quadrant of the abdomen, surrounded by adhesions which produced a complete pyloric obstruction. In addition, there was a large subphrenic abscess and a necrotic liver. Unfortunately, the patient was in very poor condition and died seventy-two hours postoperatively.

SUMMARY

A case is presented in which a preoperative diagnosis of sponge in the abdomen was made and verified. The diagnosis was based on persistence of a small, localized collection of small bubbles of air trapped in the mesh of the sponge. The collection of air is in a circumscribed area, the bubbles of gas are smaller and more uniform in size than intestinal gas, the gas bubbles are not surrounded by a limiting membrane and there was no change in the appearance when the patient's position was shifted and on separate days. If the diagnosis is considered, it is unlikely to be mistaken for anything else. These films were shown to Dr. Daniel Kornblum,[4] Radiologist at the Harvey Cushing Veterans Hospital in Massachusetts. About a year later he had the opportunity to see a similar case and diagnose it correctly early in a stormy postoperative course. His patient survived.

This report is rendered in the belief that if the diagnosis of sponge in the abdomen is considered and looked for, others may have the opportunity of making this important diagnosis before too much damage ensues.

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PYOPNEUMOHEPATITIS

A CASE REPORT

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PYOPNEUMOHEPATITIS is an abscess of the liver consisting of a cavity containing pus and gas, and presenting the characteristic fluid level appearance. A survey of the literature reveals only 2 reports of liver abscess with gas. Golden,[3] in his two volumes on Roentgenology, mentions that he has seen 1 case of gas in a liver abscess. R. S. Smith,[9] in 1944, reports 1 case of liver abscess with pus and fluid level with a concomitant abscess of the right lower lobe of the lung. In 1938 Ochsner, DeBakey and Murray[8] reviewed the subject of liver abscess and failed to report a case of pyopneumohepatitis.

The following case report is interesting because of its rarity and its biochemical and bacteriological implications:

A white adult male, barber by occupation, aged sixty-one, had enjoyed good health with the exception of an attack of acute appendicitis twenty years ago, which was cured by operation. In September, 1945, he consulted the writer because of experiencing vague abdominal pains. Roentgen studies of the biliary and gastrointestinal tracts demonstrated the presence of multiple diverticula of the transverse and of the descending colon. Under medical treatment he enjoyed good health until November, 1947, when he began to feel weak and listless. He continued to work, although in the afternoons he noticed unusual fatigue and had bouts of chills and fever. He consulted several physicans without any amelioration of his condition. In March, 1948, he complained of vague discomfort in the epigastrium. Again the biliary and the gastrointestinal tracts were subjected to roentgenological studies. A diagnosis of a penetrating carcinoma of the stomach with a large metastasis in the liver was made (Fig. 1, 2 and 3). On March 26, 1948, the patient again consulted the writer. Hospitalization was advised preparatory to an exploratory laparotomy. He was admitted to the Lutheran Hospital of Manhattan. Two days following his admission, his temperature chart revealed a septic type of fever. The possibility of a subphrenic collection of pus was considered and further roentgen studies were ordered. With the patient

FIG. 1. Note defect in the lesser curvature of the stomach and area of decreased density in the right lobe of the liver.

placed in the upright, right lateral recumbent, and left lateral recumbent positions, the films of the right upper quadrant and lower right chest demonstrated the presence of a large abscess cavity with a fluid level and gas. (Fig. 4 and 5). Blood examinations were essentially normal except for a leukocytosis and mild secondary anemia. Urinalysis was negative. The patient was placed on antibiotic therapy and a transthoracic approach operation planned. On April 6, 1948, the patient was brought to the operating room and under inhalation anesthesia, segments of the eighth and ninth ribs on the right side were resected.

FIG. 2. Note what appears to be a penetrating lesion of the lesser curvature of the stomach.

FIG. 3. Note round area of decreased density and calcific deposits in the right lobe of the liver, interpreted as a metastatic lesion.

FIG. 4. With patient in an upright position, there is an area of decreased density and fluid level. Also note the thickness of the liver border surrounding the cavity.

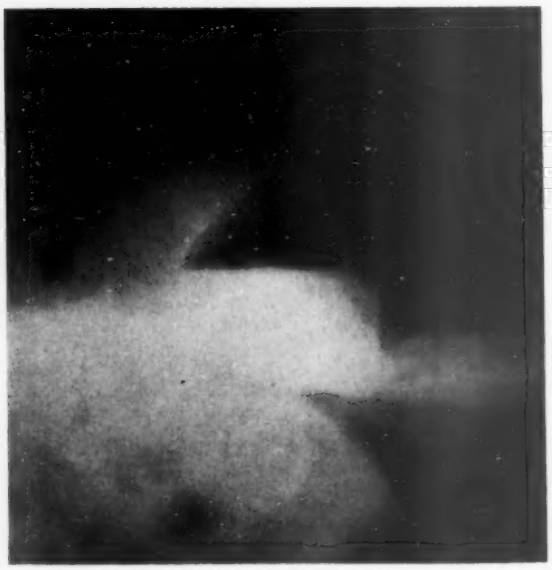

FIG. 5. With patient in the left lateral recumbent position, note the change in fluid level and the thickness of abscess wall.

There were no adhesions between the parietal and visceral pleurae and the chest cavity was inadvertently opened. Streptomycin was placed in the pleural cavity and the opening was closed. The diaphragm was incised and again the absence of adhesions between the dome of the liver and diaphragm were noted. The subdiaphragmatic space was walled off with guaze and an aspirating needle inserted into the dome of the liver. Pus and gas were obtained. The puncture wound was enlarged and the pus was evacuated. The cavity was dusted with streptomycin and packed with gauze. The wound in the chest was left open and packed with iodoform gauze. Supportive and antibiotic therapy was continued. The patient made an uneventful recovery and was discharged on May 14, 1948.

Bacteriological studies of the pus revealed a pure strain of *B. coli* communior.

Comment. The pathogenesis of liver abscesses has been clearly expounded by Ochsner *et al.* In brief, the infecting agent may be blood borne; may be an extension of a cholecystitis or a cholangitis; the infection may reach the liver through the portal system from the appendix, colon, or rectum. Trauma may be the causative factor from penetrating wounds or subcutaneous injuries Bacteriological and parasitological studies of the pus may reveal the presence of pure strains of organisms or mixed infections. The purpose of this report is not to indulge in a discussion of amebic or echinococcus infestations, but to discuss the role played by the organism of the Escherichia tribe. *B. coli* is found widespread in nature and predominates in the gastrointestinal tract of man. It is aerobic and facultatively anaerobic. It is a gas producer and at temperatures of 45 and 46° C. on glucose media, both carbon dioxide and hydrogen are liberated. The fecal odor is imparted to the gas when hydrogen sulphide is liberated from protein fermentation.

With this bacteriological phase of the report in mind, let us comment on the biochemical aspects of the case. In 1843, Claude Bernard, the brilliant French physiologist, conducted experiments on the functions of the liver. He was the first to demonstrate that glucose was taken from the blood stream and converted by the liver into glycogen, and as the occasion arose, the liver reconverted the stored glycogen into glucose and through the hepatic veins liberated it into the blood stream. This process was called glycogenesis and glycogenolysis. He also showed that in the living liver there was little or no glucose, and that only after death the unstable glycogen was quickly changed into glucose.

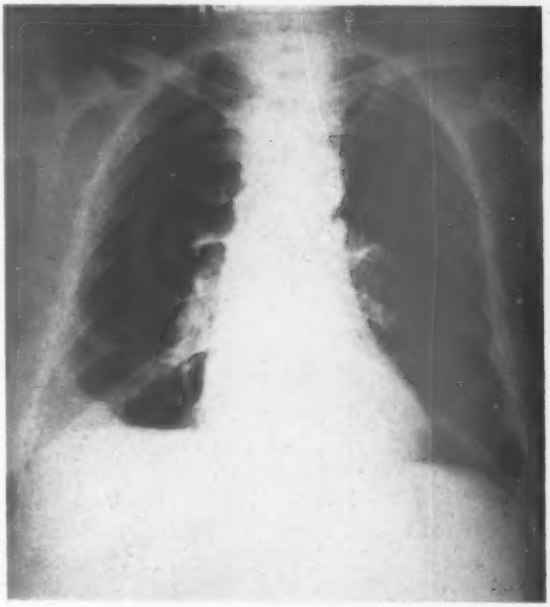

FIG. 6. The appearance the right chest and dome of the liver four months postoperatively.

Since these mutations took place in the liver cells, it was argued that an endocellular substance initiated the changes. To these substances were given the name of enzymes. It is of interest to note that reducing sugars, such as fructose and glucose, must first be phosphorylated by a phosphorylase. This is then followed by polymerization of the monosaccharide. The glycogen exists in the liver cell in combination with phosphorus. It is this substance which is acted upon by a specific hepatic glucophosphatase as one of four important phases in carbohydrate catabolism.

Four months after operation, roentgen studies of the gastrointestinal tract were

Fig. 7. Note shadow of diverticulum of the jejunum superimposed on that of the stomach. Four months postoperatively.

Fig. 8. Diverticulum of the jejunum shown clearly defined from the outline of stomach shadow.

again conducted (Fig. 6, 7 and 8) and the roentgenograms show that what had been interpreted as a malignant lesion of the stomach was in reality a diverticulum of the jejunum. We can only conjecture that the cause of this patient's abscess was an embolic phenomenon from the multiple diverticula present in his gastrointestinal tract. Also, that the chronicity of the infection in the liver permitted biochemical and bacteriological reactions leading to the formation of pus and the production of gas in the abscess cavity.

CONCLUSION

A case of pyopneumohepatitis is presented. It is rare and of great interest. The treatment is surgical and in this case the outcome was favorable.

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MELORHEOSTOSIS LÉRI

REVIEW OF LITERATURE AND REPORT OF A CASE

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THE discovery of the roentgen rays half a century ago, and the subsequent progressive perfection of roentgenography revealed a host of unsuspected abnormalities of osseous structures. In 1922 Léri and Joanny[12] described a previously unreported anomaly, noting an unusual distribution of hyperostosis dispersed down the side of the bones of an extremity, somewhat resembling the tallow drippings down the side of a candle. To this "flowing" hyperostosis down the limb they gave the name "melorheostosis" (μέλος—limb; ῥέω—to flow).

In 1925 Lewin and MacLeod[15] reported a similar case, admittedly uncertain of their classification as a type of osteosclerosis. When Muzii[17] reported the next case in 1926, he made no attempt to catalogue it. The first author to investigate the histopathology by biopsy was Putti,[19] who reported the fourth case in 1927, suggesting that it be called "osteosis eburnans monomelica" (hardening of the bone involving a single limb). In the same year Zimmer reported the fifth case, also describing the microscopic picture, but he preferred to call the condition "osteopathia hyperostotica condensans."

Having carved its niche in medical literature, case reports have continued to appear with persistent regularity, but it soon acquired the faults so common to the medical literature of any unusual anomaly: (1) case reports improperly included (Hall,[5] Hilton[7]); (2) cases uncatalogued or described as a new entity (Horwitz[8]); (3) erroneously reported as different entities (Geschickter,[4] Wakeley[24]); (4) inclusion of "hearsay" cases (unpublished, observed elsewhere by others, vouchsafed as accurate case compilation; Carpender,[1] Kraft[10]). Melorheostosis is of sufficient rarity to warrant reporting every discovered case. Unlike some other osseous anomalies of unsymptomatic nature which are uncovered purely by accident, melorheostosis has a specific syndrome demanding differential diagnosis from similar conditions having a different prognosis, or requiring some specific therapy. Before presenting our own case and our tabulation of the available case reports, we wish to describe the syndrome and discuss its etiological and clinical aspects.

SYMPTOMS AND SIGNS

The degree of symptomatology depends entirely upon the location, the extent, and the activity of the pathology. Since the condition is purely local, there are no generalized constitutional manifestations, Although it is possible for a case to be discovered by accident before the onset of any symptoms, pain is the commonest complaint, and is present in practically every case. It may vary from a vague "feeling" to a sharp penetrating ache, but it is rarely severe, and never constant. The vague boring nature with remission on rest is characteristic.

When the condition has started early in life, abnormal curvature of the involved bone, with or without shortening of the limb, may be present. When the process extends beyond the smooth confines of the periosteum, stony swellings and deformities may become palpable and obvious, and the limb may feel heavier and appear comparatively larger than the opposite one, despite any concomitant muscular atrophy. Pressure on the local nerves and blood vessels has resulted in paresthesias, neuralgia, venous congestion, and edema. There is usually free motion at the joints, since the pathologic process skips over any

intervening joint space, but motion may be restricted by mechanical obstruction (thickening of the contiguous articular surfaces or heteroptic ossification in the para-articular structures), to the point of immobilization without actual ankylosis.

DISTRIBUTION AND DIAGNOSIS

The descriptive prefix "mel" and the term "monomelica" were bestowed by early authors to indicate that the condition was confined to a single extremity. However, reports of cases occurring in both limbs, or in other portions of the skeletal system, force us to abandon these terms entirely or relegate them to a qualifying subdivision. With few exceptions, however, all the cases have been confined to all or part of a single limb. There is in addition a characteristic selectivity for only one side of a bone (the femur or humerus), or to a single bone where two lie parallel (either tibia or fibula; radius or ulna). Where the process continues down into the carpus (or tarsus) to the phalanges, only a linear segment is affected. The extent of involvement reported has been dependent upon how early the case was first observed, and with what rapidity the pathology progressed, and it has varied from as little as a single digit[20] or a small segment of the lower end of the femur, as in our own case, to the involvement of all four limbs[16] or of both lower limbs, part of the pelvis, lumbar spine, and skull.[1]

Since the microscopic findings (see below) are not pathognomonic, diagnosis is dependent upon the roentgen ray alone. The early roentgen appearance is one of irregular thickening of the inner border of the cortex of one side of a bone. The roentgenogram may show this dense hyperostotic irregular linear mass apparently within the marrow, but rotation of the limb with exposures taken in several planes will reveal the margin of origin. At the onset, only the inner margin of the hyperostotic mass is irregular, but at later stages the process penetrates or distorts the smooth confining contour of the periosteum. The appearance of the local joint remains unchanged even when the process is present on both opposing sides. Several cases have been reported with heteroptic deposits of the same dense calcareous strips in the adjacent soft tissues, particularly in the region of a joint.

The replacement of structural reticulation by a dense stony opacity with its peculiar patchy linear distribution and selective localization to a single side of a bone or to one of paired bones, having the characteristic contour of a coarse, irregular wavy outline, resembling the wax drippings down the side of a candle ("bougie en coulée") are specifically diagnostic. It may be (and has been) confused with some of the other hyperostotic bone conditions such as osseous lues, osteosclerosis (Albers-Schönberg disease), osteopoikilosis, osteitis deformans (Paget's disease), osteitis fibrosa (von Recklinghausen's disease), osteitis fibrosa disseminata (Albright's disease), polyostotic fibrous dysplasia, myositis ossificans, osteogenic neoplasm or carcinomatosis, chronic osteomyelitis, traumatic or infectious ossifying periostitis, or non-suppurative (Garré's) ossifying periostitis.

HISTOPATHOLOGY

Several authors have reported upon the microscopic appearance of biopsy material obtained from their cases. Their separate reports may give the cursory reader the impression that there is a wide variation in the individual descriptions made of the microscopic findings, but there are a few points common to all of them. The haversian system, however distorted and bizarre, remains as the basic histologic pattern, usually compacted but occasionally rarefied. There is an entire absence of any inflammatory process. Fibrotic infiltration of the trabecular structure of the bone, and fibrotic replacement of the marrow is regarded by the majority of authors (with the notable exception of Putti[19]) as the fundamental or essential primary pathology.[25] Estimations as to the proportion of osteoblasts to osteoclasts has differed widely, and it was the opinion of Junghagen[10,11]

that the condition has alternating osteoblastic and osteoclastic phases. Except for the common findings of fibrosis and absence of inflammation, the remaining histopathology reported has been dependent upon the degree of activity, the phase present, and the portion of bone from which the biopsy was taken. It will be recognized that a similar microscopic appearance is present in several of the other hyperostotic bone conditions, each of which is usually regarded as a separate distinct clinical entity. Fairbank,[3] Watson-Jones,[25] and others, have commented at length upon this striking similarity of the histopathologic picture present in the various seemingly separate and distinct entities, suggesting a probable relationship of the basic pathologic process, despite any etiologic differences.

ETIOLOGY

Microscopic examination of biopsy material has revealed no clue to the etiology. The selective localization of the pathology does not follow the anatomic distribution of either nerves or blood vessels. Age is not a factor (cases having been observed from infancy to senility), and there is no preponderant incidence in either sex. With a single exception, all authors have denied a hereditary or racial trait. The only significant clue is the occasional association of a scleroderma with exactly the same distribution. Several etiological hypotheses enthusiastically advocated in the past are no longer tenable, such as a specific or parasitic infection (Léri, Loiseleur, and Lievre[10,11]), endocrine (Meisels[10,11]; Goldschlag[10,11]), and subperiosteal telangiectasis (Moore *et al.*[10,11]).

Zimmer[26] explained the pathology on the basis of an embryonic metameric disturbance, conceiving that the dysplasia of a minute segment of the mesoderm of the embryonic somite which enters into the formation of a single limb-bud, would, by its size and position, determine the location and extent of resultant pathology along an exact axial distribution. This ingenious hypothesis is attractive because it sounds glib, it has an authoritative, factual connotation, and it is difficult or impossible to disprove; moreover, it has no scientific basis or proof; it explains only the distribution and not the actual pathology.

Putti[19] regarded the pathology as the result of local vascular obliteration produced by neurosympathetic vasomotor stimulation. The roentgenologist is well acquainted with the increased density found in the osseous architecture following vascular curtailment. It is now well known and accepted that an increase in blood supply to a bone (hyperemia) will result in osteoporosis (decalcification), and conversely a decrease in blood supply produces an increase in the density of the bone (hyperostosis). The conception that the periosteum possesses any specific osteogenic function has long been exploded,[13] along with idea that the osteoblast is endowed with any special power to lay down bone. The osteoblast is merely an enlarged active fibroblast, within which inorganic salts may be deposited, as it may with any mesenchymal tissue.[25] The deposition of lime salts is a physical phenomenon under the general influence of endocrines and the local control of enzymes (phosphatase) on the chemical balance of tissue fluids. Diminished vascularity resulting from any of many causes (vasoconstriction, thrombus, embolism, low metabolism, physical occlusion by torsion, kinking or pressure) leads to local asphyxia with attendant fibrosis and fibrous replacement. Calcification is known to take place in fibrous tissue of impaired vascularity (myositis ossificans, chronic osteomyelitis, luetic osteitis from endarteritis obliterans, avascular necrosis in sequestra and ununited fractures). This sequence of impaired vascularity, fibrosis, phosphatase activity and calcification, may at times be reversible.[25]

PROGNOSIS AND TREATMENT

Because of its insidious onset, slow progress with periods of temporary or permanent arrest (but never reversal to normal bone), the disease tends to be chronic. Malignant degeneration does not occur.

Unlike some other hyperostotic conditions, pathological fractures have never been reported; this may be explained by the characteristic partial involvement (one side of a bone, or one of a pair), retaining the normal bone as splintage, and also by the fact that the sclerotic replacement of the

FIG. 1

haversian system, however distorted, is on a lamellar pattern, thereby retaining its resilience. The pain yields to rest and physiotherapy. In long-standing cases limitation of joint motion can hardly be avoided, and operative removal of mechanical obstructions may be considered. We await with great expectation the report of some venturesome surgeon who will dare resect en masse (like a sequestrum) an early locus of the pathology.

CASE REPORT

F. DeN., male, aged thirty-one, native born electrician of Italian parentage, was seen first in July, 1947, complaining of a dull ache in the left knee which he attributed to a trivial twist while at work. There was no swelling, external evidence of injury, nor any restriction

FIG. 2

of motion at the knee, but the constant boring nature of the pain, with so trivial an injury led to roentgenographic examination. This revealed the presence of a dense shadow, 2 by 7 cm., lying along the cortex of the medial side of the lower end of the left femur. This opacity showed a smooth periosteal border, and an ir-

regular wavy inner border. He recalled having had pain in the knee ever since he hit it against a rock in January, 1945, while on combat duty in France, when he was thrown to the ground by the blast of a shell which exploded about 15 feet overhead. He continued on active service, receiving no treatment, although he continued to complain of intermittent pain. No roentgenographic examination was made of the knee until a year later, in January, 1946, when he was released from the armed forces. Many attempts to obtain these films from the Army Medical Department and the Veterans Administration for examination and comparison have been unsuccessful. The patient's complaint and disability yielded to a short course of diathermy, but it has recurred at intervals for short periods. Re-examination by roentgen rays some thirteen months after showed no change from the initial appearance (see Fig. 1, 2, and 3).

FIG. 3

CASE COMPILATION

Although several previous authors had made extensive reviews of the subject, Kraft[10] began a chart of the cases reported, listing some 16 cases in 1932 and augmenting the chart to 19 cases the next year.[11] By 1943 Hall[6] expanded this chart to 40 cases but he somehow left out Sante's case (which Sante had never reported but which he diagrammatically published in all the editions of his textbook[20] as a typical example of the condition, while permitting Kraft[11] to print the actual roentgenograms). Moreover, Hall's own case[6] and that of Hilton[7] have been rejected by several

Year	Author	Limb	Age	Sex	Remarks
1939	Fairbank[3]	Right and left lower	16	M	Wakeley's case[24]
1941	Stutz[21]	Pelvis	59	M	
1941	Müller-Alberti[16]	Right and left, upper and lower	8½	F	First noted at 5 yr.
1941	Kibby[9]	Left lower	5	F	
1941	Horwitz[8]	Left lower	27	F	Not reported as melorheostosis
1943	Carpender *et al.*[1]	Right and left lower	10	F	Plus lumbar spine
1943	Clément and Combes-Hamelle[2]	Left upper	9	F	Scleroderma in exactly same distribution
1946	Nunez[18]	Right upper	48	F	Biopsy made; skull also involved
1946	Le Vay[14]	Left lower	9	M	
1947	Trivelli[23]	Right lower	7	F	First noted at 3 yr.
1948	Spiegel and Koiransky	Left lower	31	M	

authors (with whom we agree) as not being actually cases of true melorheostosis. To the acceptable remaining 39 cases hitherto charted, we have reviewed 10 additional case reports in the available literature, bringing the total number of cases, including our own, to 50. We are curtailing our bibliography in the interests of space and brevity, and are merely supplementing the chart originated by Kraft[10,11] and continued by Hall.[6] The reader is referred to their articles for the remaining literature.

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RADIOLOGY IN THE MEDICAL SCHOOL*†

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AS THIS is the last meeting of the American College of Radiology at which I shall appear as your president, I very gladly embrace the opportunity which it offers to express to you my deep sense of gratitude for the liberal education my association with the College has provided.

As chairman of the Commission on Education, as one of the Chancellors, then as chairman of the Board of Chancellors for four years, and finally as the twenty-fifth president of this great organization, I have had an experience which I shall cherish forever.

The American College of Radiology was organized in 1923, and it has already celebrated a quarter of a century of service to medicine in general and to radiology in particular. This period has been one filled with new frontiers in diagnosis and therapy; new developments in radiological equipment; new tools, the radioactive isotopes, for research, for diagnosis, and for radiation therapy; new problems in war and peace; more concern with public relations, and increased efforts to develop ethical relationships between the radiologists and the hospital. It has been during this period that we have learned something about the implications of the loss of free enterprise, the increasing strength of those who would provide compulsory planned economy and Federal control of medicine. New conditions, it is claimed, require new remedies. Now is the time for you and me to use the "compass of history" to chart our course on the sea of the future.

In the beginning, there were twenty-one radiologists selected as Charter Fellows. There was only one class of membership, and that was Fellowship. With the growth of radiology and the development of certain trends, it became apparent to some of the members that the American College of Radiology should assume a more important role concerning certain facets of our specialty. As a result, the program was enlarged and now the American College of Radiology is dedicated to support those broad fundamentals of the educational and economic aspects of radiology which will provide better medicine for our people and proper representation for radiologists. In order to perform such functions our Constitution and By-Laws have been changed and modified from time to time.

Our By-Laws now provide for several classes of membership. We have a total membership of 2,063 Members and Fellows. The categories of membership include: Members, Fellows, Honorary Fellows, Members Emeritus, Fellows Emeritus, Associate Fellows, Life Members and Fellows, Retired Members and Fellows, and Associate Members.

Today we are able to speak as never before for American Radiology. Our College enjoys an enviable position among medical organizations of this country and is recognized everywhere as a strong, effective and smoothly working institution with high principles and ideals.

One of the interests of the College is concerned with education, and as you know, a part of the February meeting of the College is set aside for "Teachers in Radiology." Tonight we are gathered together for our annual convocation and it has seemed appropriate that I discuss briefly the place of radiology in the university. It deserves thought and planning if radiology is to fulfill its obligation to society.

President Conant, in his oration at the formal exercises of the Harvard Tercentenary Celebration on September 18, 1936, stated: "From the first foundations to the present, four main streams have watered the soil on which universities have flour-

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† Presidential Address before the American College of Radiology, Atlantic City, N. J., June 5, 1949.

ished. These ultimate sources of strength are: firstly, the cultivation of learning for its own sake; secondly, the general educational stream of the liberal arts; thirdly, the educational stream that makes possible the professions, and lastly, the never-failing river of student life carrying all the power that comes from the gregarious impulses of human beings."

President Conant was speaking for the university as a whole, but his remarks are just as applicable to radiology. The discovery of the roentgen ray and of radium and the production of radioactive isotopes are three of the great advances of all times. A man cannot become a competent physician unless he has some knowledge of these agents and their uses. All three of them are embodied in the field of radiology.

Radiology in many of our medical schools is a separate department and as such is headed by a professor. Radiology not only serves every branch of clinical medicine, but it has an equal opportunity to serve the pre-clinical sciences—anatomy, physiology, physiological chemistry, pharmacology, and pathology. The professor of radiology, therefore, must be concerned with teaching in the pre-clinical and clinical years of our undergraduate medical students. The scope of his activities should include participation in fundamental investigation, experimental and clinical. It is essential that the professor be an experienced medical radiologist, one "with a scientific discipline, giving exactness to habits of thought and tempering the mind with that judicious faculty of distrust which can alone . . . make him wise."[2]

In some of our medical schools very little time was or has been provided for radiological teaching. There is a great opportunity for the radiologist to assist in teaching anatomy, physiology and pathology to students in their first two years of medicine, and clinical radiology in their last two years. These courses, when planned with the other departmental professors, provide the student with useful information and are very popular. This plan is recommended to those schools where such courses are not included at present in their curriculum.

There should be a department of radiology in the medical school, preferably not in any of the existing sections. It should be a place where different interests converge and draw from each other's store of knowledge. The department of radiology should be not only a consultant branch but a service department, and if properly staffed and with an ample budget, it will be able to provide the various pre-clinical divisions a better opportunity to carry on research in animals and humans. Such scientific cooperation will accomplish more and will confer greatness on the institution. There are many brilliant examples of such cooperative ventures, one of the more recent being the observations of Barclay and his co-workers at the Nuffield Institute in Oxford.

To accomplish any such program requires vision, understanding, and support. Osler in his address at McGill University Medical School, October 1, 1894, said that a University has two functions—Teaching and Thinking. By thinking, Osler meant that it is the duty of the professional corps to enlarge the boundaries of human knowledge—the sort of thinking that alone enables the university to exercise a wide influence on the minds of men.

"Teachers who teach current knowledge are not necessarily investigators; many have not had the needful training; others have not the needful time. The very best instructor for students may have no conception of the higher lines of work in his branch, and contrariwise, how many brilliant investigators have been wretched teachers!"[3]

In a school which has reached a stage where it wishes to provide opportunities for higher university work and "wishes to do thinking as well as teaching, men must be selected who are not only thoroughly au courant with the best work in their department the world over, but who also have ideas, with ambition and energy to put them into force—men who can add, each

one in his sphere, to the store of the world's knowledge."[3]

One of the chief difficulties of achieving such an opportunity in our medical schools for the young teachers and investigators is an adequate budget. Medical colleges do not have adequate budgets for many of their present needs. The radiological equipment is expensive. It requires space which is often at a premium. Advanced work, teaching, investigation and clinical duties require an adequate number of assistants.

Presently such a program would be new in many schools. Most of the professors of radiology receive their salaries or income from clinical departments in teaching hospitals. This clinical work oftentimes has first call upon their time. It too is altogether likely that many of the administrative heads of teaching hospitals will not be tempted to participate in the budget necessary to carry on radiological activities in the medical schools. There are some who will. They must show the way. Then, too, it will be necessary for the professor of radiology to seek financial assistance from his patients and friends of the institution. Each pre-clinical and research department should set aside a part of its budget to assist in underwriting essential radiological needs. There are certain foundations that may provide assistance.

Finally, radiologists doing private practice in those communities in which medical schools are located will do well to allocate a part of each day to assisting in hospital or medical school radiology. The pattern for such assistance has long been conventional in surgical and medical departments. It is up to you and to me to do what we can to help put radiology in the medical school where it can do for teaching and investigation in the pre-clinical years what has been done so well in the clinical years.

My friends, the future of radiology can be bright. It is still young and there is still much to be learned. It is a great specialty in the greatest of all professions. By far the most dangerous foes we have to fight are apathy, indifference, carelessness and self-satisfaction. Beware, lest we fall heir to these faults.

There is a delightful Arabian proverb—

> "He who knows not, and knows not that he knows not, is a fool. Shun him.
> He who knows not, and knows that he knows not, is simple. Teach him."

And, too, you remember the wonderful allegory of Dante, by which he conducts us through the three stages of human existence. In the Inferno we witness the misery of sin; in Purgatory, the struggles of virtue. Those who have labored up the hill—who have surmounted the temptations of this world and begun to taste the pleasures of the next, are described as enjoying that peace of mind which is imaged by the terrestrial Paradise. Dante compares himself to a pilgrim, who arrived at last before the temple he has long desired to see, surveys it with fond delight, in the hope of being able, on his return home, to communicate to others the glories he has witnessed.[1]

We in radiology can, like Dante, be pilgrims and by precept, example, and hard work, show our colleagues what radiology has to offer in the medical school. If we do not, it will be done by others. Already research divisions in medicine, surgery, and other specialties are establishing radiological facilities within their departments completely divorced from the main department of radiology. There are many things in radiology needful of our attention, but none more important.

Challenge begets progress. In the course of a bare half century the profession of radiology has achieved progress that is without parallel in any other branch of medicine. But each year new challenges present themselves, and perhaps the greatest of all is near at hand. Our first duty as disciples of the scientific discipline we have adopted for our professional career is to constantly advance the art and science which gives us a common bond and unites us in our endeavors. Our greatest usefulness lies ahead of us; our future awaits

our making. It may be a great future; it may be a disillusioning one. In our hands is the making of it. Our destiny depends upon the course we chart and upon our constancy to our high purpose. The course and the destiny of man's aspirations may be altered by the will of men and the inspired example of our leaders.

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MULTIPLE MYELOMA

II. VARIABILITY OF ROENTGEN APPEARANCE AND EFFECT OF URETHANE THERAPY ON SKELETAL DISEASE*†

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MULTIPLE myeloma is a much studied malignant disease usually classified as a form of subleukemia. It results from the proliferation of abnormal plasma cells within the bone marrow. The cause of the cellular proliferation, as in malignant growths generally, is unknown. The clinical features of the disease relate to four types of abnormalities: (1) anemia due to replacement or alteration of the hemopoietic tissues by the proliferating plasma cells; (2) demineralization of the bones that house red marrow; (3) the production of abnormal serum and urinary proteins, and (4) renal disease[2,5,6,9,16] (Chart 1).

Multiple myeloma was once considered a rare disease, but it is now being diagnosed more frequently. In institutions where patients with skeletal disease, chronic anemia, obscure fever, and renal disorders of uncertain origin are routinely studied hematologically, with the generous employment of bone marrow examinations, multiple myeloma is relatively common. In our institution, its recent incidence has been roughly two-fifths that of Hodgkin's disease, or one-half that of myelogenous leukemia.

Multiple myeloma has been a uniformly progressive and fatal disease. Evidence of real spontaneous remissions or lasting cures is lacking. The average time of survival after the diagnosis is once made has been one to two years. Some individuals succumb in a month or two, while others have lived for ten or more years.

The therapeutic agents commonly employed in the treatment of leukemias and malignant lymphomas have failed to alter significantly the clinical course of multiple myeloma. Roentgen irradiation has been used most extensively.[2,4,5,6,7] It is mainly effective in the treatment of local lesions and in relieving bone pain. Radioactive phosphorus and nitrogen mustard compounds have usually been of little or no benefit.[8,13,14,17,18] Stilbamidine, pentamidine, and antimony compounds alleviate pain and produce basophilic granulation in the cytoplasm of the abnormal plasma cells.[16] Skeletal recalcification has been observed in some patients. The essential features of the disease, the presence of numerous abnormal plasma cells in the bone marrow, hyperglobulinemia, proteinuria, etc., and its ultimate clinical outcome, however, are not altered.[12,15,16] The use of these drugs is limited by serious toxic reactions.

Patterson, Ap Thomas, Haddow and Watkinson[11] reported their study of the therapeutic effect of urethane (ethyl carbamate) in leukemia and other malignancies in 1946. Two patients with multiple myeloma were included in their series. They observed, in agreement with some later authors, no improvement after the use of urethane. Alwall[1] observed, however, in one patient with multiple myeloma a strikingly beneficial effect after urethane was given over a longer period of time. This suggested the need of a more extensive and prolonged study of the effect of this chemical in multiple myeloma. Loge and Rundles[10] studied 4 patients treated with urethane during observation and follow-up

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periods ranging from seven to thirteen months. A selective beneficial effect exceeding that obtainable by other therapeutic agents was observed. Fever and skeletal pain subsided within a few weeks. Abnormal plasma cells decreased in number in the bone marrow and underwent morphologic changes indicative of retarded or arrested growth. In individuals with severe anemia immature granulocytes and nucleated red cells disappeared from the circulating blood. The blood values subsequently improved or became normal. Serum protein abnormalities and Bence-Jones proteinuria became less pronounced or disappeared.[3] Serial roentgenograms of the skeleton showed no progression in the destructive lesions, and after four to six months there was the beginning of skeletal recalcification.

The present report summarizes at the end of two years a continuation of this study in a group of patients now numbering 24. The general beneficial effects of urethane therapy on the different manifestations of multiple myeloma continue to be observed. The variability of the roentgenologic features of the skeletal disease, and its course following urethane therapy are the aspects of our study to be presented in particular detail at this time.

The current status or final outcome of 24 consecutive patients diagnosed as having multiple myeloma at our hospital during the course of this study is indicated in Table 1. Eight patients could not be treated with urethane or could only be given inadequate amounts of the chemical. Two of them died a few hours after admission before specific therapy was started. Five

TABLE I

MULTIPLE MYELOMA, DUKE HOSPITAL, OCTOBER, 1947–SEPTEMBER, 1949. NEW CASES: 24

		Case No.
No specific therapy	2	15—Died, 36 hours, anemia, anasarca
		23—Died, 2 hours, congestive failure
Urethane therapy incomplete	6	2—Died, 3 weeks, pneumonia
		8—Died 3 weeks, acute shock
		9—Intolerant of urethane
		10—Died 7 days, uremia, pneumonia, interstitial glomerulonephritis
		12—Died 5 weeks, myelitis, convulsions
		17—Died 4 weeks, hypertensive heart disease

Urethane therapy: 90–270 grams 2 months to 1,850 grams in 18 months: 16 patients

Case No.	Therapy Begun	Result	Present Status
1	10/21/47	Excellent	Well and working
3	2/23/48	Excellent	Died 10/23/48, Postoperative pelvic plasmocytoma
4	3/ 3/48	Good	Well, worked regularly. Relapse
5	4/12/48	Palliation	Died 10/18/48, irregular therapy
6	7/ 2/48	(Spinal plasmocytoma)	Disease generalized, good responses, well
7	8/ 1/48	Excellent	Well and working
11	11/10/48	Pain relieved	Improved. Recurrent infections
13	2/ 7/49	Improved	Usual household activities
14	2/ 9/49	No benefit	Ascites, hepatitis. Died 8/31/49
16	4/23/49	Still well	No symptoms before therapy
19	4/12/49	Excellent	Resumed full time work. Later relapsed
18	5/18/49	No benefit	Little response first 3 months, died 10/17/49
20	6/ 2/49	Excellent	Active. Asymptomatic. Relapse Jan. 1950
21	6/14/49	Excellent	Postoperative laminectomy. Active, well
22	8/ 6/49	Palliation	Uremia. Temporary improvement, died 1/6/50
24	8/17/49	Excellent	Acute myocardial infarction, died 1/9/50

died in seven days to five weeks before much benefit from therapy could have been expected. In all of these grave symptoms had been present for months or years before they were admitted to the hospital, and treatment attempted without the correct diagnosis being established. One patient died of acute circulatory failure of a type that has since been combatted successfully in other patients by energetic fluid, plasma and blood infusions. One patient became persistently intolerant of urethane after she had been given the chemical for several days without having it diluted abundantly with food or fluids.

Sixteen patients have completed one or more courses of urethane. The clinical benefits attributable to this therapy have been very satisfactory in nine. Three others have had gratifying relief from skeletal pain, although one of them died after six months of irregular treatment and one elderly individual continues to be incapacitated by recurrent pulmonary infections. One patient in whom myeloma was discovered before symptoms had developed has been treated and remains well. Two patients apparently derived no benefit from taking urethane and one was possibly made worse since she developed persistent ascites soon after it was discontinued. Although we believe that some patients already have had their lives definitely prolonged by therapy, their over-all survival will require some years of study to determine.

Pain resulting from skeletal disease is the symptom that usually leads to the diagnosis of multiple myeloma, but this was the presenting symptom in only two-thirds of our patients. Anemia led to its discovery in 3 instances, proteinuria or renal disease in 3 patients, and spinal cord tumors requiring laminectomy for decompression in two. In 3 individuals with generalized bone marrow involvement there was no roentgen evidence of skeletal abnormality. In 6 patients the initial symptoms and findings were those of localized bone tumors or destructive lesions, and in 2 there was pronounced diffuse demineralization easily confused with metabolic osteoporosis. Two individuals in this series had laminectomies in other hospitals for ruptured intervertebral discs before the presence of myeloma was recognized. The range of skeletal involvement in these patients is illustrated by the following cases:

Case 12. This man, white, aged seventy-seven, farmer, had convulsions for five years and pain of increasing severity in his neck, right shoulder, and arm, with sensory impairment in the latter for two years. He lost weight from his usual 175 pounds to 154 pounds.

Roentgen films showed osteolytic destruction of the right halves of the sixth and seventh cervical vertebrae (Fig. 1 *A*) and collapse of the second lumbar vertebra but no definite skeletal lesions elsewhere. Examination of the peripheral blood showed no abnormalities. Sternal puncture showed that 63 per cent of the cells were abnormal plasma cells. The urine contained 1.0 to 2.8 grams of Bence-Jones protein per twenty-four hours. The serum calcium, phosphorus, alkaline phosphatase, serum albumin and globulin levels were all normal. His spinal fluid protein was elevated to 300 mg. per 100 cc.

After admission to the hospital his convulsions continued, and confusion and disorientation became worse. His legs became paralyzed and the sensations impaired. He was given 90 grams of urethane during three weeks in the hospital, but was then discharged home, contrary to advice. He died two weeks later.

Case E. L. B. (C-8222). This sixty-three year old farmer had had disabling back pain for four months. On examination the physical findings included induration of the prostate gland typical of carcinoma. Roentgen films showed an osteolytic lesion in the body of the tenth thoracic vertebra which was interpreted as an osteolytic metastasis (Fig. 1*B*). Orchectomy was performed.

Skull films later showed multiple osteolytic lesions. A bone marrow examination then revealed an increased percentage of abnormal plasma cells. A needle was introduced into the body of the tenth thoracic vertebra and the aspirated marrow contained large numbers of abnormal plasma cells diagnostic of multiple myeloma. He was treated with localized roent-

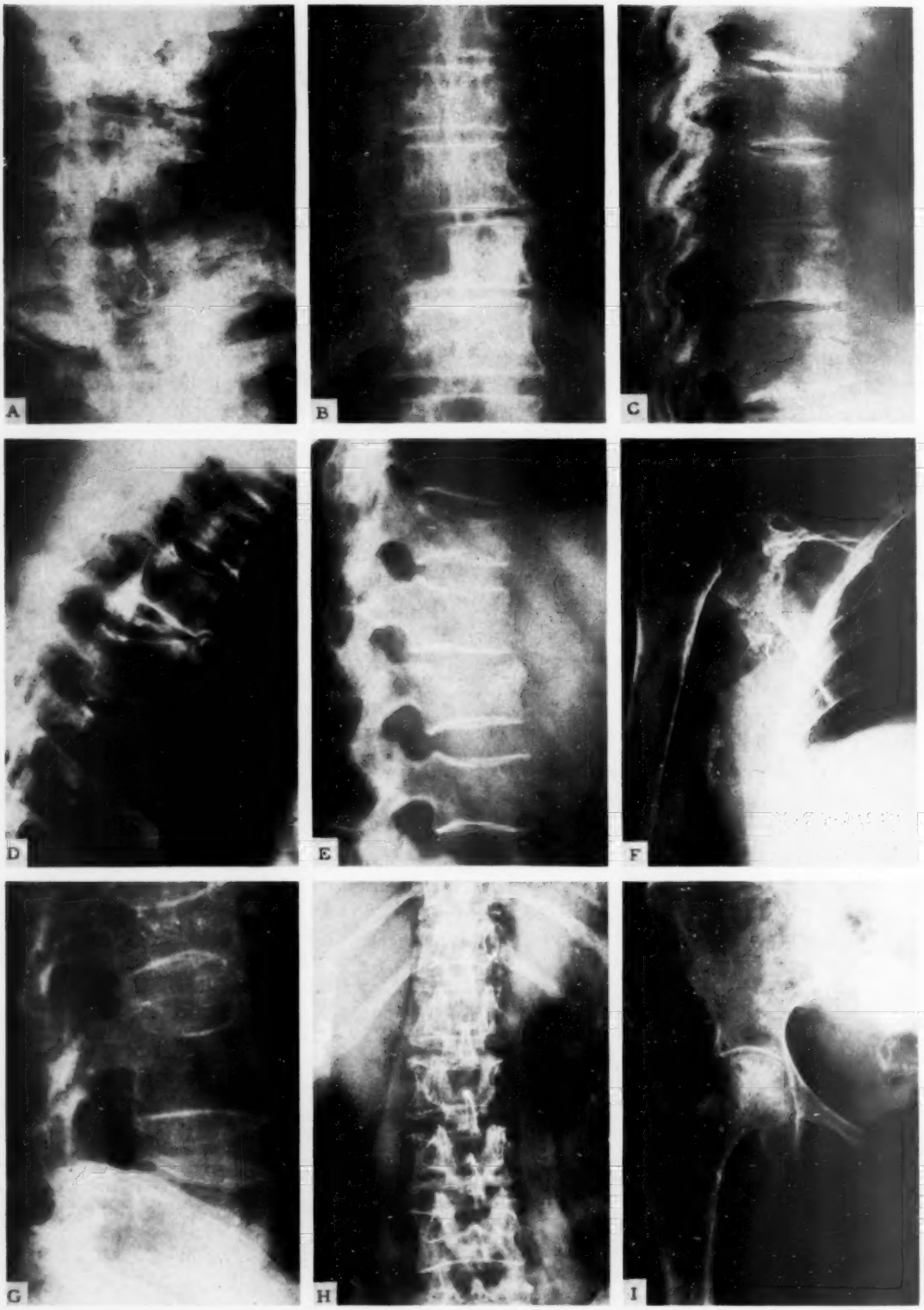

FIG. 1. Variation in skeletal lesions in multiple myeloma. (*A*) Case 12. Destruction of lateral portions of sixth and seventh cervical vertebrae. (*B*) and (*C*) Case E. L. B. (C-8222). Osteolytic lesion in lateral portion of body of the tenth dorsal vertebra. (*D*) Case 21. Wedging of sixth thoracic vertebra with extradural plasmocytoma producing spinal cord compression. (*E*) Case 22. Demineralization and compression of the second and fourth lumbar vertebrae in patient with severe anemia and nitrogen retention. (*F*) Case 14. Destructive tumor of right scapula, rarefactions in upper humeri. (*G*), (*H*), (*I*) Case 9. Diffuse demineralization of lumbar spine, multiple areas of osteolysis in ribs, ilium, and upper femur.

gen irradiation in June, 1946, and died nine months later.

Case 21. This forty-six year old married woman had been treated for several years for arterial hypertension. For three years she had had chronic pain between the scapulae that developed following a fall. One week before her hospital admission her legs became clumsy and too weak to bear her weight. Examination showed a flaccid paralysis of the legs. Roentgen films of the thoracic spine showed wedging of the sixth dorsal vertebra (Fig. 1 *D*). There was a spinal fluid block. Laminectomy of the fifth to seventh thoracic vertebrae was performed, and an extradural tumor partially resected. The pathologic diagnosis was plasmocytoma. Examination of the peripheral blood and determinations of the serum calcium, phosphorus, alkaline phosphatase, and serum proteins showed normal values. The urine was free of protein. Seven per cent of the cells in the sternal bone marrow were abnormal plasma cells.

Roentgen films of the remaining skeleton showed small osteolytic lesions in the skull, but no other evidence of disease.

Case 22. This fifty-seven year old white farmer began four months before admission to have low back pain which became progressively more severe. During the week preceding his hospital admission he became very weak, confused, and subject to nausea and vomiting. On examination he had pronounced tenderness over the ribs and pain with all movement of his back. Roentgen films of the lumbar vertebrae showed demineralization and partial collapse of the 2nd and 4th lumbar vertebrae (Fig. 1*E*).

Examination of the peripheral blood showed the hemoglobin to be 8.1 grams, white blood cell count 6,100, red blood cell count 3,070,000, hematocrit 26 per cent, average red cell volume 84 cubic micra, and reticulocytes 1 per cent. Seventy per cent of the cells in the sternal marrow were abnormal plasma cells. He excreted in the urine 10–12 grams of protein daily which gave the qualitative tests for Bence-Jones protein. The blood non-protein nitrogen was 55 mg. per 100 cc., serum calcium 13.3 mg., phosphorus 5.1 mg. per 100 cc., alkaline phosphatase 3.2 Bodansky units, serum albumin 4.0 grams, and globulin 2.0 grams per 100 cc.

Roentgen films of the skeleton showed in other areas only large and small osteolytic rarefactions in the skull.

Case 14. This fifty-three year old merchant's wife developed pain in the right scapula one year before her hospital admission, and noted for six months a gradually enlarging tumor in this area. Roentgen films showed partial destruction of the lower scapula (Fig. 1*F*) and a fracture through a lesion in the fifth rib posteriorly on the left. A needle aspiration of the scapula tumor showed great numbers of abnormal plasma cells. Examination of bone marrow aspirated from the sternum showed 6 per cent abnormal plasma cells.

Examination of the peripheral blood showed the hemoglobin to be 10.0 gm. per 100 cc., white blood cell count 4,100, red blood cell count 3,580,000, hematocrit 34 per cent, average red cell volume 94 cubic micra, and reticulocytes 1.5 per cent. The circulating white blood cells were normal in type and in percentage distribution. The serum calcium was 8.1 gm. per 100 cc., phosphorus 3.4 mg., and alkaline phosphatase 1.0 Bodansky unit. The total serum proteins were 8.1 grams per 100 cc., with albumin 3.4 grams and globulin 4.7 grams. An electrophoretic analysis of the serum showed a peak in the gamma region comprising 47 per cent of the total protein.

Roentgen films showed in addition to the scapula tumor, rarefactions in the upper humeri, and small osteolytic lesions in the skull.

Case 9. This married woman, white, aged fifty-three, developed chronic back pain after lifting a baby six months before her hospital admission. After her first clinic visits and hospital study she was thought to have postmenopausal osteoporosis. Examination of the peripheral blood showed normal values. The serum calcium was 9.3 mg. per 100 cc., serum phosphorus 3.0 mg., and alkaline phosphatase 4.2 Bodansky units. The total serum proteins were 7.4 gm. per 100 cc., albumin 4.5 gm. and globulin 2.9 gm.

Examination of the sternal bone marrow showed 11 per cent of the cells to be abnormal plasma cells. The urine contained 0.04–0.2 gm. of Bence-Jones protein per twenty-four hours.

Roentgen films showed, in addition to pronounced diffuse demineralization of the lumbar and thoracic vertebrae (Fig. 1*G*), small osteolytic lesions in the ribs, skull, pelvis, and femora (Fig. 1, *H* and *I*).

Case 15. This colored woman, aged forty-nine, developed low back pain radiating into her legs fourteen months before her admission

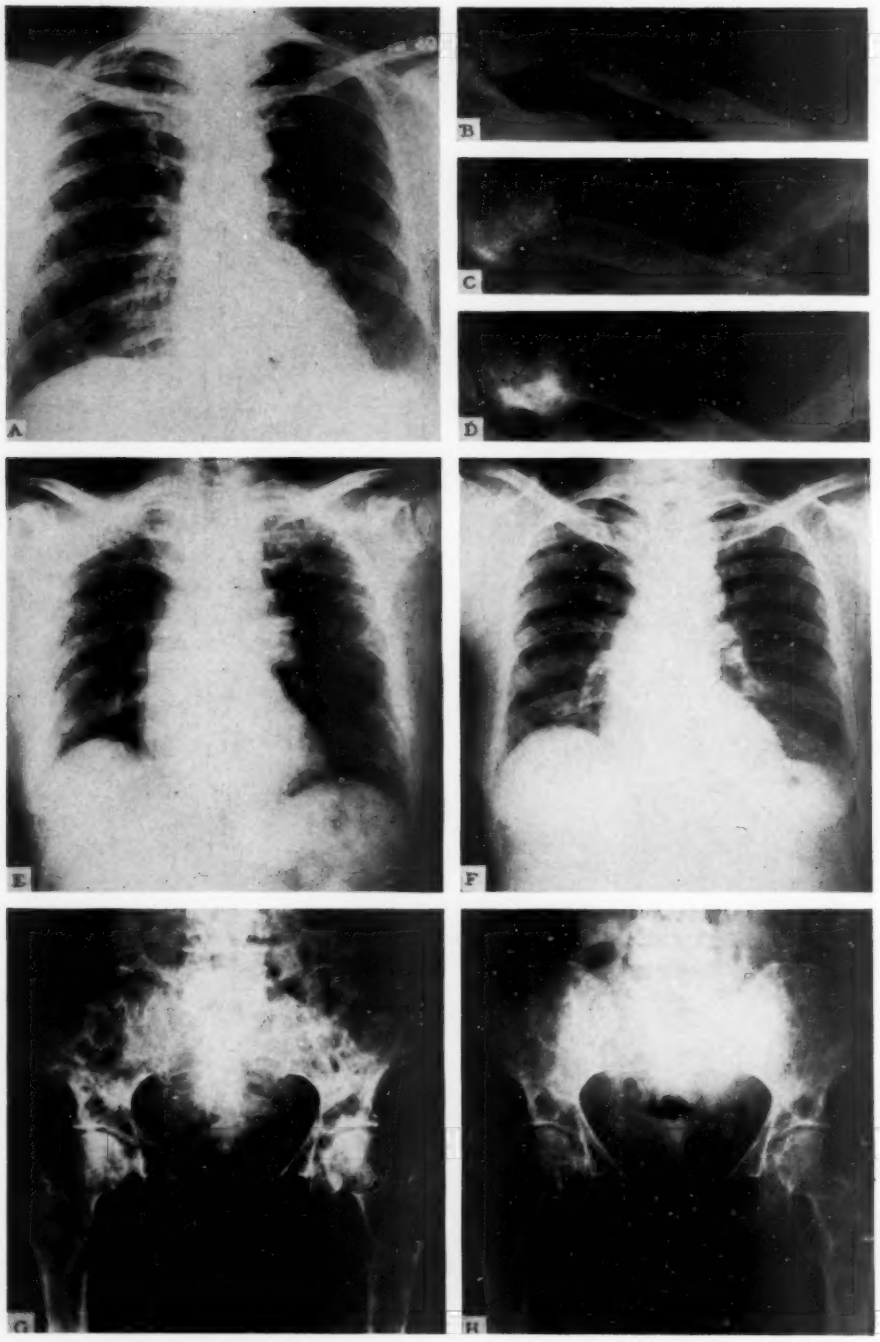

FIG. 2. (*A*) Case 15. Dissolution of third ribs anteriorly and of ninth rib on right. Effect of urethane on skeletal disease in multiple myeloma. (*B*) Case 19. Film of distal clavicle showing fracture, callous formation, and areas of rarefaction. (*C*) Film seven and one-half months later showing growth of bulbous tumor, incomplete fracture and increased areas of rarefaction medially. (*D*) Film five months after beginning of urethane therapy showing increased bone density and reduction in size of tumor. (*E*) Case 3. Chest film taken March 1, 1948, showing osteolytic rarefactions and demineralization of ribs. (*F*) Chest film taken November 15, 1948, showing recalcification of ribs with virtually normal bony architecture. (*G*) Case 3. Film of pelvis and upper femur taken March 15, 1948, showing generalized, patchy areas of osteolysis. (*H*) Film eight months later showing conspicuous increase in bone density and reduction in size of the osteolytic lesions.

to the hospital. After a few weeks of symptoms an operation with spinal fusion was performed. She was not benefited by this and developed progressive weakness, an anemia treated with repeated blood transfusions, generalized skeletal pain, and finally anorexia and vomiting. She was admitted to the hospital with severe congestive heart failure and generalized edema. Severe anemia and hypoproteinuria were present. Examination of the bone marrow showed overgrowth with abnormal plasma cells. She died suddenly thirty-six hours after admission of circulatory failure.

Roentgen films showed a fused lumbar spine, irregularity of the fourth lumbar vertebra, the disappearance of both third ribs anteriorly and destruction of the ninth right rib posteriorly (Fig. 2*A*). Films of the skull showed no lesions.

After a few weeks of successful urethane therapy, bone pain occurring at bed rest usually subsided and patients began to tolerate cautious physical activity. By four to six months patients with severe skeletal disease became ambulatory and able to work. During this process hypercalcemia subsided and there was often some elevation of the serum alkaline phosphatase activity. The alterations in the roentgenologic appearance of the skeletal disease during the months following urethane therapy are illustrated by the following 3 patients:

Case 19. This physician, aged forty-two, noted tenderness about his shoulders in the fall of 1948. He fractured the right clavicle after a slight fall (Fig. 2*B*), and a few weeks later fractured a rib when coughing. Low back pain with radiation to the left foot developed. In January, 1949, he fell and fractured his left clavicle. On January 28, 1949, a laminectomy for the removal of a suspected intervertebral disc compressing the fourth lumbar nerve route was performed. Convalescence was slow, and two months later another rib was fractured by a trivial stress. The acromial ends of the clavicles continued to become more prominent and roentgen films showed an irregular tumor with areas of bone destruction on the right (Fig. 2*C*). In April, 1949, a biopsy of the left clavicle led to the pathologic diagnosis of a plasma cell tumor.

Examination of the peripheral blood showed no abnormalities. The urine contained only the faintest trace of protein. Determinations of the serum calcium, phosphorus, alkaline phosphatase, serum albumin and globulin levels were all normal. The sternal bone marrow contained sheets of abnormal plasma cells.

Roentgen films of the skeleton showed osteolytic lesions in the skull, healed rib fractures, and small osteolytic lesions in the shafts of the femora in addition to the clavicular tumors.

Between April 12 and June 30, 1949, he took 300 gm. of urethane by mouth. Before therapy was complete he was able to return to part time work, and six weeks after its discontinuation he was working full time without symptoms or complaints. Roentgen films of the right clavicle five months after the beginning of therapy (Fig. 2*D*) showed reduction in size of the tumor, increased calcification and firm union with the clavicle. Increased calcification was also evident in the left clavicle. Skull films at this time showed some regression in the osteolytic lesions.

Case 3 (C. F. H., B-5150). The details of this patient's illness and her course during the early months of therapy have been previously reported.[10] Before therapy was begun she was confined to bed in constant distress due to extreme skeletal disease. There was generalized demineralization of the skeleton with large and small areas of non-reactive destruction in the ribs, vertebrae, pelvis, long bones and skull (Fig. 2, *E* and *G*, and 3*A*). After a few weeks of therapy she became free of pain and ambulatory. Serial roentgenograms showed after four months the beginning of recalcification. A chest film eight months after the beginning of therapy showed recalcification of the ribs and restoration of normal bony architecture (Fig. 2*F*). Marrow aspirated from the sternum and from the ribs at this time was virtually normal. A segment of rib removed for histopathologic study showed no definite bone lesions. Roentgen films of the pelvis (Fig. 2*H*), eight months after the beginning of therapy, showed pronounced recalcification and reduction in size of the bone lesions. Serial skull films taken during this period of time showed no progression in the extensive osteolytic lesions; and the margins of bony dissolution became gradually less sharply outlined, representing, perhaps, a tendency for recalcification (Fig. 3, *A* and *B*).

Case 1 (A. R., C-19679). The details of this patient's illness and early response to therapy

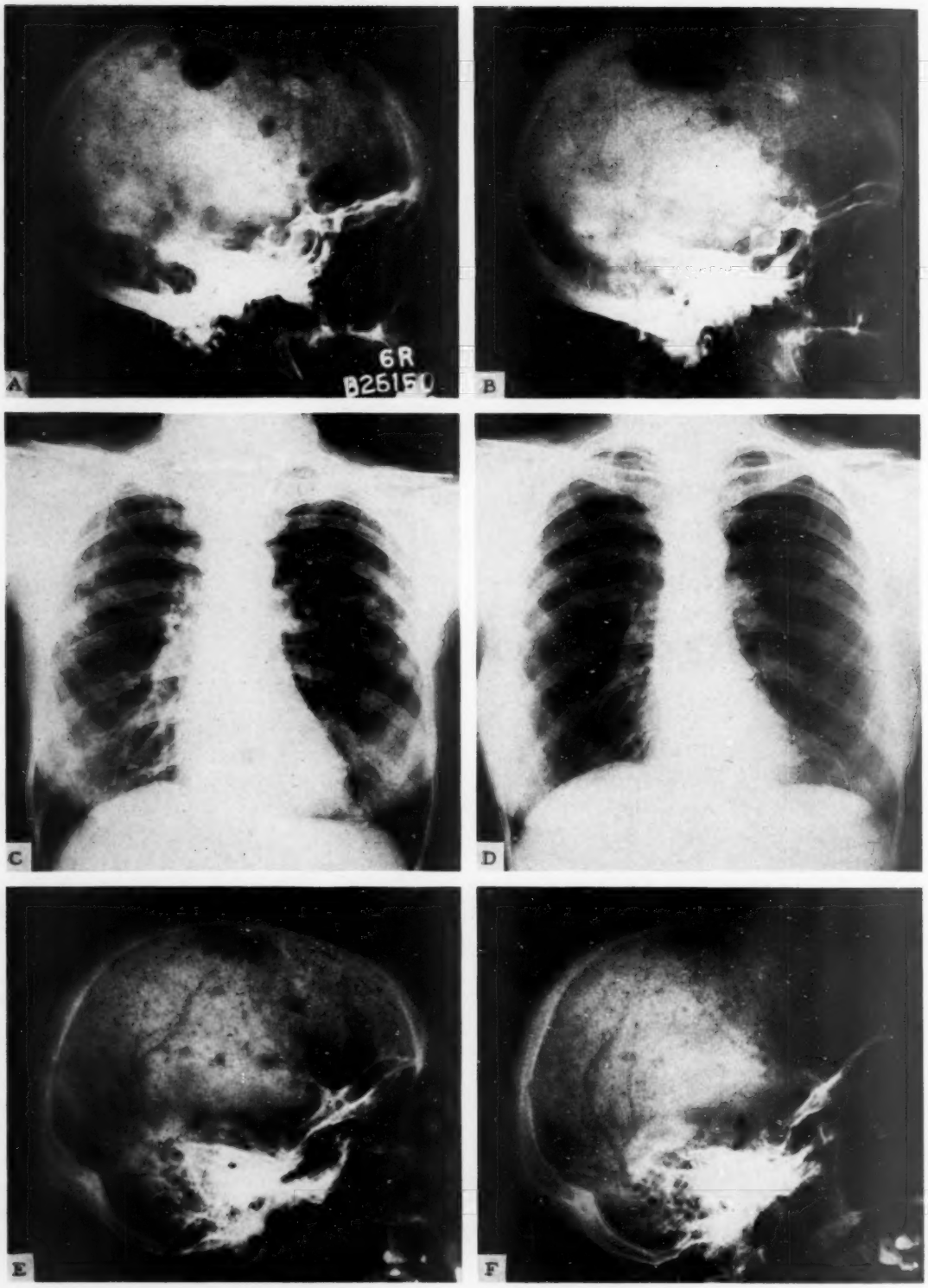

FIG. 3. Effect of urethane on skeletal disease in multiple myeloma. (*A*) Skull film, Case 3, February 19, 1948, showing multiple areas of bone destruction. (*B*) Skull film nine months later showing no progression in bone lesions but little or no evidence of recalcification. (*C*) Case 1. Chest film taken October 15, 1947, showing cystic areas and spotty demineralization of ribs with healing fracture in ninth rib posteriorly. (*D*) Chest film taken August 27, 1949, showing recalcification of ribs and virtually normal bone pattern. (*E*) Case 1. lateral skull film taken October 15, 1948, showing multiple areas of osteolysis. (*F*) Skull film taken May 7, 1949, showing arrest in progression of lesions but little or no evidence of recalcification.

have also been previously published.[10] She has now been followed for nearly two years through three courses of urethane therapy. She continues to enjoy good health and works regularly.

Before therapy, roentgen films of the skeleton showed generalized destructive lesions in the skull, ribs, scapulae, spine, and pelvis. During the early months of therapy she became entirely free of skeletal symptoms. Comparison of the chest film taken before therapy with another twenty-two months later showed recalcification and restoration of virtually normal rib architecture to have occurred (Fig. 3, *C* and *D*). Comparison of skull films at similar intervals of time showed no evidence of progression in the lesions, and some haziness around their margins possibly representing a tendency to recalcification.

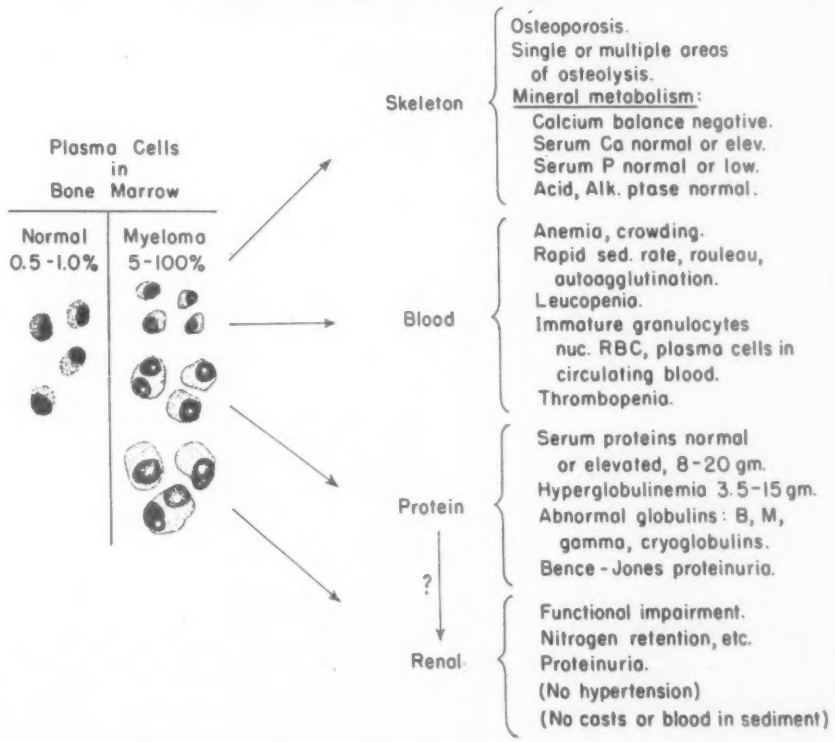

Chart I. Pathogenesis of multiple myeloma. Outline of clinical abnormalities resulting from abnormal plasma cell proliferation within the bone marrow.

DISCUSSION

The osteolytic skeletal disease, such a prominent feature of multiple myeloma, although commonly widespread, is essentially a localized bone disorder. Anatomically the bones that contain red marrow are affected. Histopathologically, the bone trabeculae adjacent to nodules of proliferating plasma cells are demineralized first. Marrow aspirated from areas of skeletal dissolution usually contains a very high percentage of plasma cells, while that obtained elsewhere may contain relatively few. Plasma cell proliferation may occur in isolated areas, in multiple areas, or diffusely throughout the marrow. The roentgen appearance of this disease, accordingly, ranges from isolated lesions to multiple lesions or may be only that of diffuse demineralization.

When the disease is actively progressing, calcium is mobilized from the skeleton and the calcium balance is negative. With rapid demineralization there may be hypercalcemia. Since the serum phosphatase activity is normal or only minimally elevated, there should be no confusion in diag-

nosis, however, with hyperparathyroidism. Calcium metabolism during urethane therapy has not been studied, beyond the observation that hypercalcemia subsides and alkaline phosphatase activity rises slightly as the process of skeletal repair goes on. Serial roentgenograms of the affected bones have shown little convincing evidence of repair during the first three months of therapy, even in patients who were once in distress due to advanced skeletal disease who have again become free of pain and ambulatory. By four to six months, recalcification and the reappearance of trabecular pattern in bones subject to weight bearing and other stress has been definite. Residual abnormalities of architecture will no doubt persist about fracture sites and large cystic areas. In most instances the skull lesions have shown no progression after therapy but little tendency to heal during the period of observation to date. Serial roentgenograms of the skeleton thus have obvious limitations in judging response to therapy. This is ordinarily managed in terms of other findings related to the disease.

The effect of urethane in multiple myeloma represents an encouraging advance in its practical therapy. The long term results and the length of survival of patients that may be expected in the future will require further study. About one-third of our recent patients have been referred for diagnosis and treatment so late in the course of their disease that effective therapy was not possible. An early diagnosis of this disease has become for the first time a matter of practical importance to the afflicted individual. The range and variability of the roentgen appearance of the skeletal abnormalities have been emphasized with the hope that early and accurate diagnosis will be promoted. In patients with osteolytic lesions in the bones that contain red marrow it is necessary to search for other evidences of multiple myeloma, bone lesions not productive of symptoms, anemia, abnormal proteinuria, hyperglobulinemia, and so forth. Examination of bone marrow aspirated from the usual sites, or from the lesions directly, ordinarily leads to conclusive diagnostic findings.

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DISCUSSION

Dr. T. Leucutia, Detroit, Michigan. As Dr. Rundles said, during the past decade our old method of roentgen therapy in multiple myeloma has been supplemented by various new methods. He mentioned this morning those used more recently, especially radioactive phosphorus, nitrogen mustard gas therapy, and diamidine therapy, but there are other methods. For example, in Detroit we have used for some time colloidal lead orthophosphate in conjunction with deep roentgen therapy or without the roentgen therapy, and very recently, we have tried colloidal lead orthophosphate in which the phosphorus has been made radioactive. Of course, there are still other methods described in the literature. Often, there is a remarkable relief of symptoms with definite prolongation of the useful life of the patient from these remedies. Yet it is generally recognized that all have a very limited value when the problem of a clinical cure is considered.

It is fortunate that Drs. Rundles and Reeves have devoted their painstaking efforts to trying to explore the therapeutic efficacy of another new remedy, urethane, which lately has created such interest in conjunction with the treatment of leukemias and lymphomas. I, perhaps, may add here that we have treated an impressive number of cases of leukemias with urethane but the results were not altogether satisfactory so that at the present time we only use it exceptionally in that particular disease.

Drs. Rundles and Reeves have studied in minute detail the changes which occurred in the skeletal system, blood, serum protein, and in relation to renal function. They have established very useful criteria indicative of the immediate and late prognosis of multiple myeloma. Then by making these criteria the basis of their investigations, they have evaluated the immediate effect of urethane by measuring the improvements in relation to all aspects of the disease. During a period of less than two years, they were able to treat a total of 24 cases of multiple myeloma, a fact which considering the rarity of the disease, must, in itself, be considered a remarkable accomplishment. The essayists presented their findings in a clear, concise manner, being careful to confine their claims of success within the boundaries of possibility that one may expect in a condition as serious as that of multiple myeloma.

Evidently, a much longer time will be required before final conclusions can be drawn as to the true value of the method. I cannot but express my greatest admiration for the untiring efforts of Drs. Rundles and Reeves in a field fraught with almost insurmountable difficulties. The paper was well conceived, logically organized and well presented.

Dr. Harold W. Jacox, New York, New York. I would like to ask Dr. Rundles if there is any contraindication in his experience to the use of local roentgen therapy in the cases which have not responded with urethane.

Dr. Rundles (closing). I wish to thank Dr. Leucutia for his very kind remarks. We use urethane in treating individuals with chronic myelogenous leukemia with some enthusiasm. In those who can take the chemical well, the result is often very good.

What I know about stilbamidine and pentamidine comes largely from Dr. Snapper. He has studied the effect of this compound in more detail than anyone else. He tells me that about 1 in 20 of his patients with multiple myeloma have shown some recalcification of bone. The number of plasma cells in the bone marrow, the hyperglobulinemia and the proteinuria do not change. Our own limited experience with stilbamidine has not been encouraging.

In reference to Dr. Jacox's question, I think it is completely sound to use roentgen therapy for local lesions. In general, you can deliver more destructive effect locally by roentgen methods than you can by mouth with chemical methods.

We find, however, that this disease is ordinarily a generalized one. We give urethane slowly and believe we can achieve a very selective inhibition of the abnormal cells, with minimal effect on normal cells. We have refrained from irradiation in our patients simply because we wanted to make a clear-cut evaluation of what one therapeutic agent would do in one disease.

ROENTGEN THERAPY OF OSTEOMYELITIS OF THE FINGERS*†

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ONE of the most troublesome complications of a septic finger is a persistent subacute or chronic osteomyelitis of one or more phalanges or of the metacarpus. The patient may be disabled for months after the acute inflammation has subsided by a persistent discharging sinus and by pain and tenderness of the finger. Permanent disability is not rare, and, if the digit involved is the thumb or index finger, loss of occupation may result. If, on the other hand, sound healing of the bone can be secured, the prospect of obtaining a useful finger is greatly increased. Too often, in an effort to cut short the infective process, the patient is subjected to several operations at which fragments of bone are removed under the misapprehension that they are sequestra and that their presence is delaying healing. Sequestra do form in some cases and the resulting loss of bone seriously deforms the affected finger. More often the friable, decalcified bone breaks up under the persuasion of a metal instrument and fragments are pulled out. Even without the aid of roentgen therapy the bone is capable of recalcification, and an experienced casualty officer learns in time the value of conservative treatment. The process may, however, be long and tedious, and the impatience of doctor and patient may suggest amputation as the quickest way of getting the patient back to work. A method that is likely to promote complete healing and functional recovery in a matter of a few weeks is obviously worthy of attention. Such a method is available in a simple application of the knowledge of the effect of roentgen rays on inflammatory processes.

MODE OF ACTION OF ROENTGEN RAYS

In acute and chronic inflammations local cellular reaction plays a major part. The cells of the vessel walls, the adventitia cells, the cells of the reticulo-endothelium and even of the alveolar epithelium of the lungs, in short all cells of mesenchymal origin, can change into inflammatory cells. When healing takes place the mononuclear inflammatory cells change back into fibrocytes and fibrous tissue. The polymorphonuclear inflammatory cells disintegrate and are not capable of differentiation. Cells of mesenchymal origin regain the faculty of differentiation in post-embryonic life under the following conditions: (1) myelosis, (2) inflammations and (3) callus formation.

It is an obvious conclusion that roentgen rays might influence this differentiation. Before going into the study of the action on cells, the action on bacteria and vessels should be considered.

(a) *Action on Bacteria and Vessels.* No action on bacteria has been described when a small dose of roentgen rays is applied.

Cadness-Graves and Friend recently experimented on bacteria of all sorts and under varied conditions and could not find any evidence of a loss of vitality of the bacteria on agar or in broth. One would expect that an *increase* and not *decrease* of the dose would be more beneficial if bacteria were affected. *Aseptic* inflammations respond equally well to the treatment (Fukase, 1930). It is therefore justifiable to state that the action of roentgen rays on inflammation is not bactericidal.

Small wounds in the center of the cornea of animals, inflicted under local anesthesia,

* Based on a paper by the authors in *Proceedings of the Royal Society of Medicine*, 1947, *40*, 111–115, by permission of the Honorary Editors.

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heal more rapidly compared with controls (Freund, 1929). There are no vessels in the center of the cornea and the healing effect can therefore not be attributed to the action on vessels (Pendergrass and Hodes, 1941)

(b) *Action on Polymorphonuclear Leukocytes.* It is widely believed that the destruction of polymorphonuclear leukocytes is responsible for the favorable effects in the treatment of inflammation. The assumption that these cells are destroyed is based on investigations which Warthin carried out in 1905. He tried to prove that the disappearance of leukocytes in the blood stream of leukemic patients is due to destruction of leukocytes by the direct action of the rays. In exudates of the dorsal lymph-pouch of frogs, produced experimentally (Freund, 1927), an increased disintegration of polymorphonuclear leukocytes can be observed after irradiation. Disintegration of polymorphonuclears occurs, however, in any exudate, and the only effect of the irradiation is to speed up the process of pus formation—an effect that is to be expected in the early stages of such treatment.

A patient with myeloid leukemia who had numerous myeloid nodules in the skin was treated by roentgen rays. Biopsy of the nodules was performed before and after treatment (Freund, 1928). All stages of differentiation of local cells of mesenchymal origin in the skin into myeloid cells could seen, before treatment. As the result of irradiation these myeloid cells changed directly into fibrocytes and fibrous tissue. There were no young fibroblasts present; but the mononuclear myeloid cells, originating in the skin, changed, the nuclei became dense and stretched and layers of fibrous tissue surrounded them like onion skins.

Spontaneous healing of myeloid nodules does not occur. *The cure has been achieved by the differentiating action of roentgen rays.* It is a reasonable conclusion that under inflammatory conditions mononuclear leukocytes might likewise change into fibrocytes and fibrous tissues.

(c) *Action on Mononuclear Leukocytes.* The normal course of inflammation in the frog's tongue was studied (Freund, 1930). Widespread cellular activity could be seen outside the vessels, before any emigration from the vessels took place.

On the basis of these findings, it was presumed that the local growth of inflammatory cells might be controlled by prophylactic roentgen treatment and rapid repair achieved. Wounds inflicted on the skin of rabbits and partially irradiated healed quicker on the irradiated side (Fukase, 1930). Microscopic investigations confirmed the macroscopic appearances; there was an exudate in the part not irradiated, but hardly any inflammatory reaction in the irradiated zone, which healed per primam.

In order to exclude infection and to have a process that can be easily demonstrated, the traumatic inflammation of fractures was investigated before and after roentgen treatment (Fukase, 1930). The fibulae of rabbits were fractured on both sides. On the irradiated side the callus formation was *less*, but firm bony union occurred earlier. After five days the histological sections showed mononuclear granulation tissue on the control side, but fibrocytes were already present on the irradiated side. After eight days cartilage cells occurred, if not irradiated, and fibrocytes and fibrous tissue, if irradiated, in the same animal. The dose was 400 r. If the dose was increased to 1,600 r the inflammatory cells assumed after fourteen days the character of embryonic mesenchymal cells and, after three weeks, differentiation into many capillary vessels could be seen which prevented bony union for several weeks.

METHOD OF TREATMENT

N. S. Finzi and R. J. Phillips started the use of roentgen rays in the treatment of osteomyelitis of fingers at St. Bartholomew's Hospital, London, in 1939. The roentgenograms of a case treated by them are reproduced in the *British Medical Journal* of January 7, 1943. They show ex-

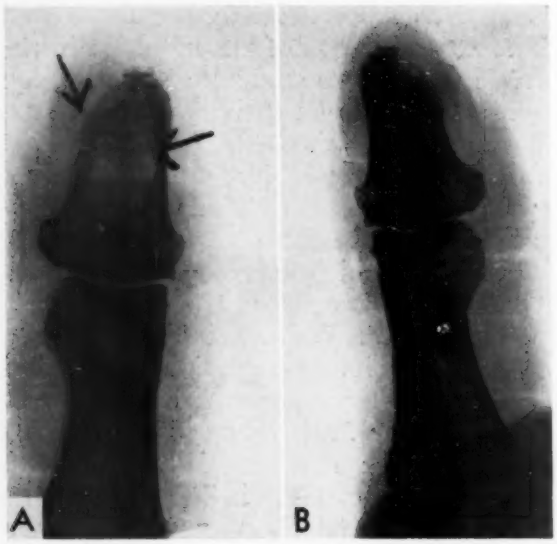

FIG. 1. Case I. (*A*) Extensive destruction of terminal phalanx. *B. coli* infection of two years' duration. (*B*) Healed after weekly dose of 50 r for six weeks.

tensive destruction of the terminal phalanx of a thumb in a case in which amputation had been decided upon. A last effort to save the thumb was made by the trial of roentgen treatment and complete regeneration was achieved. The dose used by them was 80 r, 160 kv., filtered with 0.5 mm. of copper.

We wished to apply this treatment at the Emergency Hospital, St. Albans, but were unwilling to send the patients to London during the worst of the flying-bomb and rocket attacks. We had no therapeutic apparatus available and therefore used the diagnostic equipment. It was by the use of this equipment that our results have been obtained. The septic digits were screened, using the screening voltage of 65 kv., 3 ma., and 0.5 mm. Al filter at the usual screening distance for two to three minutes once a week. Under these conditions it would take twenty minutes to administer an erythema dose; 50–75 r took two to three minutes and this dose was applied for three to five weeks. Being only 10 to 15 per cent of the erythema dose, it could not inflict burns. It is, however, important that the treatment should be carried out by an experienced radiologist since inflammatory lesions are very sensitive to roentgen rays and an excess dose might have adverse effects.

CASE REPORTS

CASE I (Fig. 1). A. B., male, aged forty-nine. On May 9, 1944, the patient was admitted to the ward on account of recurrent pulp infection of the left thumb for two years. Thumb incised and a small amount of pus evacuated. Lymphangitis is present. Culture of pus grew coliform bacillus.

On May 26, 1944, re-admitted with paronychia of left thumb. Nail removed. Lymphangitis again present.

Roentgen Finding. Extensive destruction of the distal phalanx of the left thumb.

Roentgen treatment began on June 13, 1944, and continued for six weeks. Weekly dose was 50 r.

Result. Healed in six weeks. Scar slightly painful with some horny change of skin. Wound is soundly healed and patient has returned to his work as a milker.

CASE II (Fig. 2). S. D., female, aged seventy-two. On August 2, 1944, the patient presented herself with a history of having had a septic thumb incised elsewhere on July 19, 1944.

Roentgen Finding. Osteomyelitis of the basal phalanx.

Roentgen treatment was started at once with a weekly dose of 50 r; continued for three weeks.

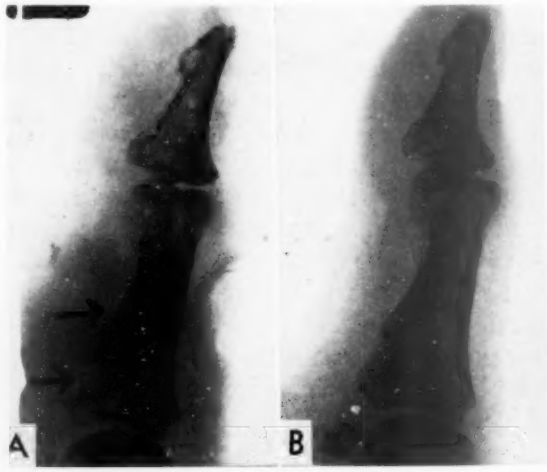

FIG. 2. Case II. (*A*) Osteomyelitis of basal phalanx. (*B*) Healed after weekly dose of 50 r for three weeks.

Result. Slight degree of arthritis of the terminal interphalangeal joint. Scar rather painful

and there is some wasting of the tip of the thumb. Function and healing are satisfactory.

Case III (Fig. 3 and 4). P. H., female, aged thirty. On July 4, 1944, the patient presented herself with history of cut on thumb seven weeks previously which became inflamed. A whitlow formed and "broke." Pus discharged. Thumb was incised at Osterhills Hospital and protruding piece of bone removed.

Fig. 3. Case III. (*A*) Osteomyelitis of terminal phalanx. (*B*) Healed after weekly dose of 50 r for four weeks.

Fig. 4. Case III. Lateral view.

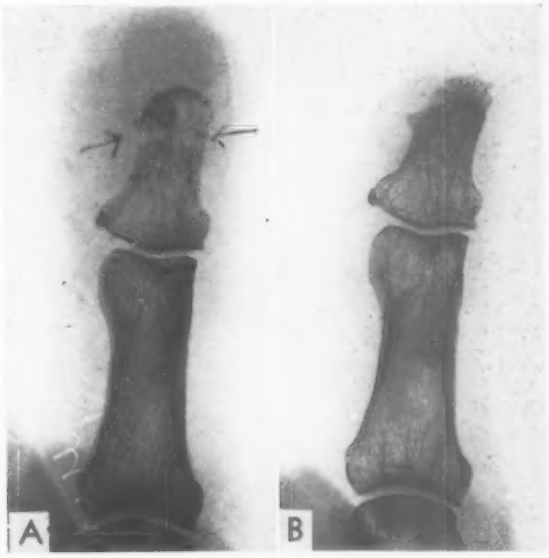

Fig. 5. Case IV. (*A*) Destruction of terminal phalanx. (*B*) Healed after weekly dose of 50 r for three weeks.

Roentgen Finding. Decalcification of terminal phalanx and piece of bone protruding through skin.

Roentgen treatment was started a few days later and continued for four weeks. Weekly dose 50 r.

Result. The thumb healed with depressed scar at tip. This was subsequently treated by a plastic operation. The thumb "goes dead" easily but is otherwise satisfactory. There is a club-like deformity, due to loss of bone substance.

Case IV (Fig. 5). A. S., female, aged forty-eight. On April 4, 1945, the patient presented herself with a history of septic thumb which had been opened a few days previously by her own doctor. There was superficial necrosis of the terminal phalanx which was not draining. Opened freely. No bone removed.

Roentgen Finding. Destruction of terminal phalanx.

Roentgen treatment was started a few days later and continued for three weeks. Weekly dose 50 r.

Result. Healing sound and slight pain in scar, function good, but limitation of movement in interphalangeal joint.

Case V (Fig. 6). E. H., aged forty-six, was admitted on March 10, 1942. The left index finger was red and swollen, with pus pointing

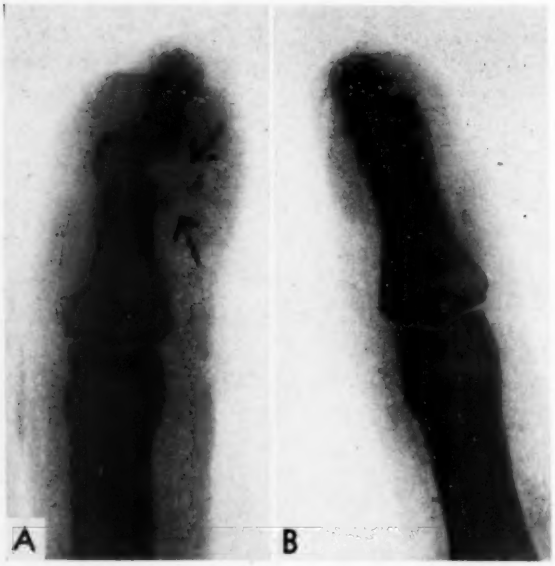

FIG. 6. Case v. (*A*) Osteomyelitis of middle phalanx. (*B*) Healed after weekly dose of 100 r for four weeks.

on palmar aspect. History was that a piece of wire wool had penetrated the palmar aspect of the tip of the finger. Finger incised on radial side from the proximal to the distal interphalangeal joints.

Roentgen Finding. April 15, 1942. Osteomyelitis of the middle phalanx and erosion of the bone on radial side.

Roentgen treatment was given consisting of a weekly dose of 100 r for four weeks (at St. Bartholomew's Hospital, London).

Result. Bone healed with limitation of movement at the distal interphalangeal joint due to partial subluxation.

CASE VI. D. E., male, aged thirty-five, was admitted on November 28, 1945. He had hit the left hand on packing case two days before admission. Abrasion became painful. Small laceration $\frac{3}{4}$ inch long was found over dorsal surface of fourth metacarpophalangeal joint. Skin around reddened. Temperature 104° F. Patient ill.

Treatment. Sulfadiazine 6 grams daily. Systematic penicillin 120,000 units for nine days. Laceration opened up. Four hourly soaks. Radiant heat. Temperature normal in six days. On December 10, 1945, the incision was enlarged.

Result. A discharging sinus.

Roentgen Finding. January 30, 1946. Marked osteomyelitis. Amputation then considered.

Roentgen treatment was started the beginning of February, with 50 r weekly for four weeks.

Result. Osteomyelitis healed. Sinus healed. Metacarpophalangeal joint ankylosed, but hand can be used for manual labor.

CASE VII (Fig. 7 and 8). N. H., female, aged fifty-three, was seen on March 19, 1946. Five weeks previously she had driven a rusty nail into the middle finger of right hand. Two weeks previously the finger began to swell and became painful and red. The finger was incised on either side of the pulp. A culture of pus resulted in the growth of *Staph. fluorescens*. Local penicillin daily through drainage tube inserted through pulp.

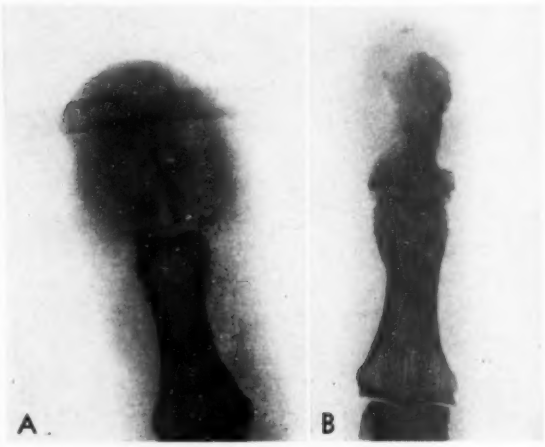

FIG. 7. Case VII. (*A*) Osteomyelitis of four weeks' duration. Organism: *Staphylococcus fluorescens*. Daily irrigation with penicillin without success. Note drainage tube at the tip of finger. (*B*) Healed after weekly dose of 50 r for five weeks.

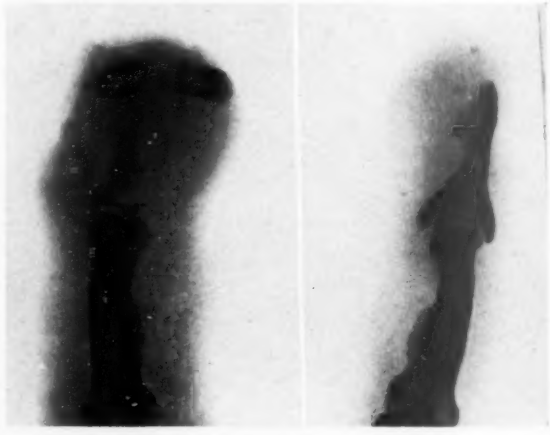

FIG. 8. Case VII. Lateral view.

Roentgen Finding. Advanced osteomyelitis of terminal phalanx.

Roentgen treatment was started on April 2, 1946, with 50 r weekly for five weeks.

Result. Small sequestrum discharged. Well healed. Movements limited.

Case viii. M. B., female, aged forty-eight, was seen on September 13, 1944. Patient had a septic thumb which was incised and pus evacuated. Three weeks later (October 6, 1944) it was still discharging.

Roentgen Finding. Osteomyelitis of terminal phalanx.

Roentgen treatment was started at once with 50 r weekly dose and continued for four weeks.

Result. Healed rapidly and movements satisfactory.

DISCUSSION

The rationale of the treatment can be explained by the experiments previously described. Debris, devitalized tissues, constitutional and nutritional causes often delay repair, long after the danger of general infection has passed. Delayed bony union can be visualized, but it is only part of the common occurrence of delayed repair. *Small doses of roentgen rays initiate repair or prevent exuberant (allergic) local reaction by their differentiating effect on inflammatory cells.* Under the mistaken assumption that bacteria or leukocytes must be destroyed, too high and too many doses may be given. Differentiation of cells takes time and requires not more than 50 to 80 r once a week. In very acute infections the dose should be reduced to 10 to 25 r. A weekly dose of 100 r should never be exceeded and not be applied for longer than eight weeks. Local and general reactions should be carefully watched and the dose adjusted accordingly.

The results were better when the treatment was started early, as then loss of bone by sequestrum formation and destruction of joints could be prevented. In 3 cases amputation, which seemed to be inevitable, was averted. The sinuses healed, the inflammation of the soft parts disappeared and the patients lost all fear of using the affected digits.

At the same time, and in a matter of weeks, the appearances of the roentgenograms changed considerably. The destroyed bone recalcified and its normal pattern reappeared.

SUMMARY

In a small series of cases roentgen treatment for osteomyelitis of the fingers was uniformly successful, confirming previous reports on the same subject.

Neither local nor general antibacterial therapy could accomplish what small doses of roentgen rays achieved.

Incapacity was considerably shortened and permanent disability prevented.

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COMPLICATIONS FOLLOWING THE USE OF NEO-IOPAX IN CEREBRAL ANGIOGRAPHY*

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THE purpose of this report is to record our experience with the use of neo-iopax as the contrast substance in carotid angiography. It was used in an attempt to find a contrast substance superior to either diodrast (35 per cent) or thorotrast. According to many authors,[2,3] neo-iopax is accompanied by fewer allergic reactions than diodrast (35 per cent), is without the radioactive qualities of thorotrast (25 per cent), and because of its greater molecular weight it has greater radiopacity.[4] The possibility of direct irritation of the vessel wall by the neo-iopax was recognized. However, it was felt that this might be overcome by injection of the substance into the rather large common carotid artery, thereby obtaining sufficient dilution of the neo-iopax to prevent irritation. The irritating effects previously reported[3,4] had all occurred after injection into much smaller vessels. In the 9 patients in our series, 4 had convulsive seizures and 1 died, soon after the neo-iopax was injected.

The selection of the patients, the preoperative medication, and the technique of injection in this series was identical with that used in a series of patients in which thorotrast or diodrast was the contrast substance (Table 1).

TABLE I

COMPLICATIONS WITH NEO-IOPAX COMPARED WITH THOROTRAST AND DIODRAST

Dye	No. Cases	No. Complications	Complications per cent
Neo-iopax	9	5	55
Thorotrast	10	1	10
Diodrast	360	4	1

The technique used is as follows: The premedication given is Na Amytal gr. iii the preceding evening and Na Amytal gr. iii, codeine gr. i, and scopolamine gr. 1/150 one hour before the angiogram. Procaine solution (1 per cent) is injected locally into the skin at the site of insertion of the angiogram needle or a cervical nerve block is accomplished with procaine solution (1 per cent). When patients are uncooperative, pentothal anesthesia is maintained. This, in a large series of patients, has been necessary in less than 10 per cent of the patients, and in the main is limited to children under twelve years of age and to adults who are disoriented because of their disease.

A No. 17 gauge needle 2½ inches long is inserted percutaneously. When percutaneous insertion of the needle into the artery is impossible, the artery has been exposed surgically and the needle inserted under direct vision. This has been necessary in 6 per cent of the patients in this series. Exposure of the artery has not varied the frequency of complications. Fifteen cubic centimeters of diodrast or thorotrast are injected as rapidly as possible (about two seconds) and roentgenograms obtained. Two and occasionally three such injections are made. When neo-iopax was used only 8 cc. was given with each injection.

An attempt was made to observe and record all irritating effects of the contrast media. Not included as a complication was the feeling of warmth or flush felt over the ipsilateral side of the face which occurs in nearly all patients.

In Table II are listed the complications observed in patients in whom neo-iopax was used.

* From the Division of Neurosurgery, Department of Surgery, University of Minnesota Hospitals, Minneapolis, Minnesota.

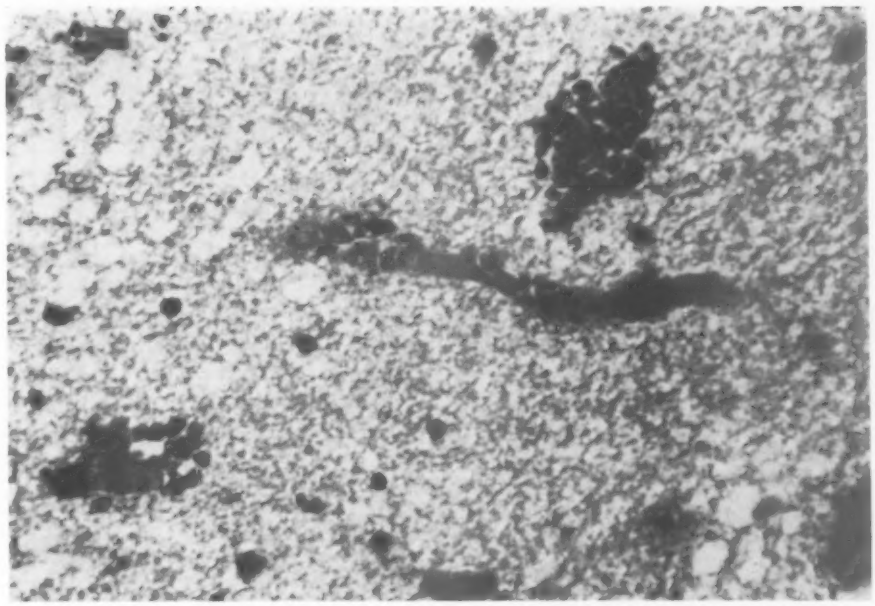

Fig. 1. Case VIII. Photomicrograph demonstrating ball and ring type petechial hemorrhages believed to be due to neo-iopax used in angiography.

DISCUSSION

In addition to the greater frequency was the greater severity of complications observed with the use of neo-iopax. Those patients having generalized convulsive seizures tended toward a state of status epilepticus and this obtained even though pentothal sedation was maintained. Autopsy examination of Case VIII revealed a cavernous hemangioma involving the vermis and the left cerebellar hemisphere. There was a necrotic area in the posterior superior portion of the right cerebellar hemisphere which was interpreted as an old hemorrhagic infarct. In addition there were, throughout the hemisphere, numerous small and large ball and ring type petechial hemorrhages; these appeared to be of recent origin (Fig. 1). These hemorrhages were considered to be secondary to the vascular irritation by the neo-iopax. Likewise it was felt that the other complications resulted from similar irritation of the blood vessel walls by the neo-iopax.

Table II

COMPLICATIONS WITH USE OF NEO-IOPAX

Case	Diagnosis	Anesthesia	Total Amount of Dye Used	Complications
I	Subarachnoid hemorrhage	Local	16 cc.	None
II	Subarachnoid hemorrhage	Local	16 cc.	None
III	Subarachnoid hemorrhage	General	16 cc.	None
IV	Subarachnoid hemorrhage	General	16 cc.	Grand mal convulsion, temporary hemiplegia
V	Thrombosis, lateral sinus	Local	12 cc.	Grand mal convulsion, temporary aphasia
VI	Subarachnoid hemorrhage	Local	8 cc.	Grand mal convulsion
VII	Subarachnoid hemorrhage	Local	16 cc.	None
VIII	Tumor, angioblastoma	General	16 cc.	Grand mal convulsion, death
IX	Subarachnoid hemorrhage	Local	16 cc.	None

No appreciable difference in visualization of the brain vascular system was noted when using neo-iopax as compared with thorotrast or diodrast. The neo-iopax was used in a 50 per cent solution which contains a 51 per cent solution of iodine and has a molecular weight of 493.

CONCLUSIONS

Neo-iopax, when used as the contrast substance in cerebral angiography, is associated with a high frequency of complications. It is felt that it should not be used for this purpose.

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AN EXPERIMENTAL STUDY OF THE CARDIOVASCULAR EFFECTS OF DIODRAST*

By ALVIN J. GORDON, M.D., SIGMUND A. BRAHMS, M.D.,†
SAMUEL MEGIBOW, M.D., *and* MARCY L. SUSSMAN, M.D.

EXTENSIVE use of diodrast solution for diagnostic purposes has resulted in reports of death and other less serious reactions attributed to the drug. While the deaths have been few in number, they nevertheless constitute a warning that the intravenous injection of diodrast is attended by a certain risk. Most of the reactions to diodrast‡ have occurred following its use in 35 per cent solution for intravenous urography but experience with angiocardiography (70 per cent solution) indicates that certain unpleasant side effects occur almost universally following this procedure. Most writers on this subject attribute the serious reactions to allergic sensitivity. The constancy of the diodrast reaction following angiocardiography, however, suggests that the drug action, of itself, could account for most of the symptoms. It was therefore decided to institute a coordinated program for the study of diodrast reactions in humans both during intravenous urography and angiocardiography, and in experimental animals. The ultimate purpose of such an investigation would be to minimize or prevent serious and unpleasant reactions to the drug.

The present report deals with the reactions of dogs to the intravenous injection of diodrast solution, and the attempts which were made to modify these reactions. Detailed observations were limited to the cardiovascular system.

Diodrast (a brand name of the diethanolamine salt of 3,5-diiodo-4-pyridone-N-acetic acid) is also known outside of the United States by the trade names of perabrodil, pelviren-D, pyelosil and pylumbrin. Other chemical names are iopyracyl, iodopyracet, and diodone. It is marketed in this country in two forms—as a 35 per cent solution (weight/volume), and a 70 per cent solution. The latter must be warmed before use, to prevent crystallization. Both concentrations were used in the experiments here reported.

Systematic studies of the pharmacology of diodrast have been previously performed. Heathcote and Gardner[4] found that the isolated rabbit heart, when perfused by a solution of 1:800 of diodrast, showed a slight increase in amplitude of pulsation, with no appreciable change in rate or coronary flow. (1:800 approximates the concentration which would theoretically occur if 20 cc. of a 35 per cent solution were diluted by the plasma volume of an average human adult (5 L.).) With a stronger solution (1:250) a much greater increase in excursion appeared, together with an increase in coronary flow. No change in rate was noted.

These authors also reported that with a strength of 1:800 diodrast, the isolated rabbit intestine showed a considerable increase in tone unaffected by atropine and therefore probably due to a direct effect on the muscle fibers.

Dogs, anesthetized by medinal, were given intravenous injections of 30 per cent diodrast in amounts varying from 100 mg. to 2 gm. per kilogram. With the larger amounts, the injection rate was slowed to about 200 mg. per kilogram per minute. A steep fall in blood pressure occurred, which, with the larger doses, amounted to as much as 60 mm. of mercury. This fall was not prevented by the previous administration of atropine. In most cases, with small doses, the blood pressure returned to its initial level within one

‡ The diodrast solution used in this study was kindly supplied by Winthrop-Stearns, Inc., New York.

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or two hours. Frequently the rise continued after this period, reaching a level 25 per cent above the original.

With larger doses, a second fall of blood pressure occurred, reaching its maximum at the second or third hour. A gradual recovery ensued, but often, even after eight hours, the original level was not attained. If a second injection of the drug was made during the period of lowered blood pressure consequent on a first injection, only very slight changes in blood pressure occurred.

In these animals, the respiration showed an acceleration and increase in depth which occurred before the blood pressure drop. With larger doses, stimulation was followed by depression; with a dose of 2 gm. per kilogram respiration ceased after twenty minutes.

Heathcote and Gardner suggested that the initial fall of blood pressure was due to both a direct action on the heart muscle and dilatation of the blood vessels.

The importance of concentration and speed of injection was recognized by Ravina *et al.*[8] who described hypotension in dogs following the intravenous injection of various contrast substances including perabrodil (diodrast), and concentrated sodium iodide solution as well as concentrated sodium chloride solution. Normal dog serum and physiological saline were innocuous.

On the basis of a limited experience, Edwards and Biguria[3] confirmed the blood pressure lowering effect of diodrast on both humans and dogs, and stated that skiodan had the opposite effect.

That the degree of vasodilatation produced by organic iodides was dependent on the vascular tone, was recognized by Kraus.[6] He found that these drugs were not capable of preventing the vasoconstrictor effects of pituitrin or of epinephrine-like compounds given in average doses to dogs, nor could they neutralize the pituitrin action at its height. However, a sharp drop of blood pressure occurred when organic iodides were given after the peak of vasoconstriction produced by these drugs had passed.

Weatherall[12] found that in concentrations greater than 1:250 diodrast increased the amplitude of the beat of the isolated auricle, increased the beat of the perfused heart and dilated the coronary arteries. The vessels of the rabbit's ear were dilated and those of the perfused dog's hind extremity showed an immediate constriction followed by dilatation and fall of blood pressure. A fall of blood pressure always occurred when diodrast in 35 per cent solution was administered intravenously to chloralosed cats (the speed of the injections was not stated). However, when spinal or decerebrate cats were used, the blood pressure usually rose, but sometimes remained unaltered.

This author explained the findings as follows: "In chloralosed cats, the fall in blood pressure is presumably due to vasodilatation, which masks the stimulating action on the heart. In spinal cats, little dilatation is possible, so that the action on the heart is apparent." Weatherall therefore challenged the hypothesis of Heathcote and Gardner that the heart was depressed by the drug.

When diodrast was injected directly into the carotid artery of cats slight disturbances of respiration and blood pressure occurred which could also be produced by injections of very hypertonic saline solutions and were attributed to the physical properties of the solutions. Sometimes there were severe reactions characterized by marked fall in blood pressure, convulsions and death.

An increase in the permeability of cerebral vessels to trypan blue, was demonstrated by Broman and Olsson[1] after injection of concentrated diodrast solutions into the carotid artery of experimental animals. A fall in blood pressure was noted, most marked in the cases in which the change in permeability was most pronounced. In these cases bradycardia also occurred.

More recently Trueta *et al.*[11] were unable to use diodrast to visualize the blood vessels and kidneys of their experimental animals because of its marked blood pressure lowering effect.

Although human reactions to diodrast are not the primary concern of the present paper, it is important to mention them briefly for comparison. Edwards and Biguria[3] stated that after an intravenous injection of 20 cc. of 35 per cent diodrast, a systolic fall of blood pressure of 15 to 20 mm. and a diastolic fall of 8 to 10 mm. of mercury was the rule. The number of observations on which this statement is based was not given.

Klein,[5] impressed by the vasodilatory effects of diodrast and uroselectan in humans, injected these drugs intra-arterially to treat certain diseases of the peripheral circulation.

In the course of perfecting the technique of angiocardiography by injecting 50 cc. of a 70 per cent solution of diodrast as rapidly as possible into an antecubital vein, Robb and Steinberg[9] made the following observations: Ten to twenty seconds after the injection the reaction began with a metallic taste and a wave of intense heat which spread throughout the body. Concurrently there was a fall of arterial pressure which rarely exceeded 30 mm. of mercury, a rise of heart rate of about 30 beats per minute, and flushing of the face and shoulders. Dizziness, weakness, nausea, sweating and pallor also occurred, but respiratory distress, cyanosis and syncope were not noted. Robb and Steinberg recommended the injection of epinephrine if a severe reaction should occur. They also searched for a suitable antagonist to the diodrast reaction. They used sodium amytal, evipal, morphine, atropine, ergotamine tartrate, pitressin and prostigmin and block of the carotid sinuses, without success.

On the basis of observations made during intravenous pyelography in 240 patients, Robins[10] classified the reactions as normal, psychogenic, autonomic or neurovascular, and allergic. Pendergrass *et al.*[7] reviewed the deaths and unfavorable sequelae to the administration of contrast media and added several new cases uncovered by a questionnaire sent out to several hundred radiologists and urologists. These authors stated that the majority of the immediate deaths were preceded by symptoms simulating those of anaphylactic shock.

Material and Methods. Nineteen experiments were performed upon 15 male adult dogs, weighing between 6 and 13 kg. Intravenous sodium nembutal anesthesia was used and the animals were given heparin to retard blood clotting and facilitate observations of arterial and venous pressures.

Arterial observations were made through a cannula inserted into the femoral or occasionally the common carotid artery. The cannula was connected directly to a strain-gauge (Statham) manometer recording on one channel of a modified four-channel, direct-writing electrocardiograph.* The manometer range was plus or minus 15 pounds per square inch. In the early experiments, the arterial pressures were recorded on an arbitrary scale, and the mean pressures measured by means of a suitably damped galvanometer. The systolic and diastolic pressures were obtained from the mean pressures by planimetric integration of the areas under the arterial curves. Later the apparatus was modified to record arterial pressures directly in absolute terms (Fig. 1).

The venous pressures were measured directly with a simple L-shaped glass tube connected to the femoral or external jugular vein by a No. 18 gauge needle. The vein was not interrupted. Injections were made into a different femoral or external jugular vein through a large cannula.

Leads one, two and three of the electrocardiogram were recorded directly on the three remaining channels of the four-channel direct-writing electrocardiograph (Fig. 1). The dogs' respirations were observed but not recorded mechanically.

Diodrast solution was given in concentrations of 35 and 70 per cent, in 10 or 20 cc. amounts, and at two different speeds—either as rapidly as possible (one or two seconds) or over a three minute period. In the majority of experiments, the drug was given as 20 cc. of a 70 per cent solution as rapidly as possible (usually in less than two seconds). It must be emphasized that this is a huge dose given at great speed. During the course of angiocardiography, an average human (70 kg.) receives 50 cc. of such a solution. On the basis of dose per kilogram of body

* The modified four-channel electrocardiograph was constructed by the Electro-Physical Laboratories, New York.

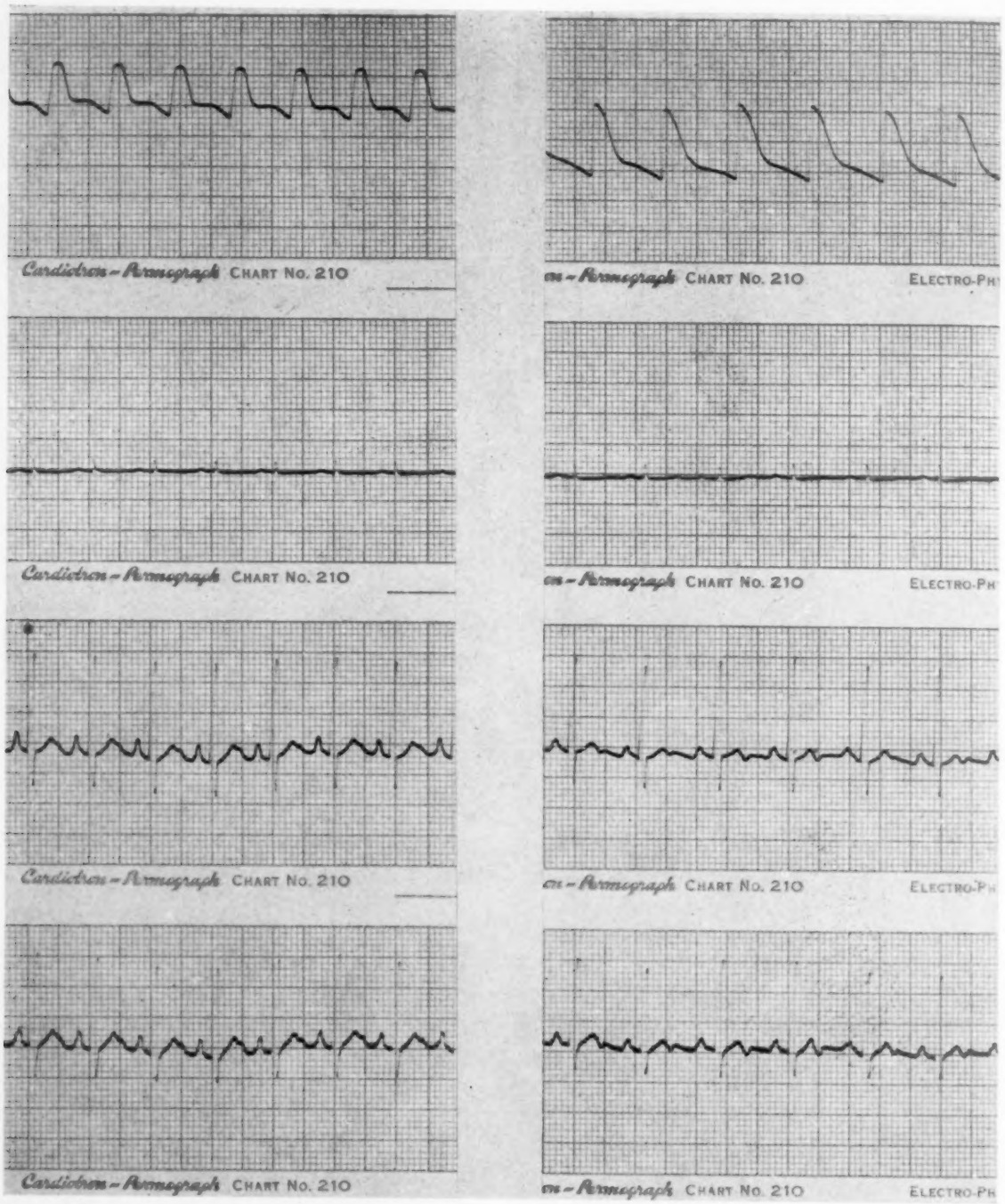
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FIG. 1. The record of a typical experiment in which a dog weighing 11.5 kilograms was given a rapid injection of 20 cc. of 35 per cent diodrast. On the left is the control period, on the right a section of the record made at the height of the diodrast reaction, twenty seconds after injection. The top channel records femoral artery pressure, the others leads one, two and three of the standard electrocardiogram. Note the changes in arterial pressures, pulse contour, and in the T waves of leads two and three.

weight, therefore, the dogs received two to four times as much drug. In addition, since in some cases a syringe with the same bore tip was used as for angiocardiography in humans, the speed of the injection was comparatively greater in the dogs.

The Typical Diodrast Reaction. The reaction of the experimental animals to rapid injection of 20 cc. of 70 per cent diodrast was characteristic and (with minor variations) reproducible (Fig. 1 and 2, Table 1). Within one or two seconds after the beginning of the injection there occurred a slight rise in both systolic and diastolic pressures without change of the arterial pulse wave contour. Between two and five seconds, there was noted a slight increase in the height of the ventricular complexes of the electrocardiogram, most marked in leads two and three followed shortly by progressive changes in the T waves and ST intervals. At about ten seconds the arterial pulse contour began to show progressive changes probably indicative of vasodilatation and reaching a maximum at thirty seconds. At ten seconds the heart rate slowed. At fifteen seconds the mean arterial pressure began to drop, the diastolic falling more than the systolic and resulting in a distinct increase in pulse pressure. The change in venous pressure was inversely proportional to the mean arterial pressure, although its rise usually preceded the fall of arterial pressure. The maximum pulse pressure occurred at twenty to thirty seconds. The mean arterial pressure, systolic and diastolic pressures usually reached their lowest at about thirty seconds, when the pulse rate was slowest. The arterial pressures returned to the initial level in most cases within about four minutes although this was variable. The pulse rate, when it returned to normal, did so within three minutes. The electrocardiogram reverted to normal within two to three minutes and the arterial pulse contour after five to ten minutes. Between ten and thirty seconds, stimulation of rate and depth of respiration often occurred although occasionally respirations slowed. Profuse salivation was sometimes noted several minutes after the injection. Flushing of the skin was often thought to have occurred but this was difficult to establish in the dogs.

TABLE I

RESULTS OF INJECTION OF 20 CC. OF 35 PER CENT DIODRAST SOLUTION INTO THE EXTERNAL JUGULAR VEIN OF A DOG WEIGHING 11.5 KILOGRAMS (VENOUS PRESSURE NOT MEASURED)

Time		Femoral Artery Pressure	Pulse Pressure	Pulse Rate	Remarks
Minutes	Seconds				
	0	166/113	53	150	Injection begins
	1.4				Injection ends
	2	180/120	60	136	T_2 and T_3 increased
	9	190/107	73	150	T waves flattening
	15	146/73	73	130	
	20	127/53	74	125	
	25	123/46	77	125	
	30	120/53	67	125	
	35	127/60	67	130	
	40	140/73	67	136	
	50	140/73	67	136	
2		146/80	66	136	
3		153/86	67	150	T waves normal
4		160/93	67	150	
5		160/100	60	150	

The Reaction in Detail: Arterial Pressures. The drop in blood pressure was always striking, the mean pressure always falling to about one-half of its initial value, the diastolic often reaching 30 mm. of mercury from an initial level of 120 mm. Although the arterial pressures usually returned to

normal within four to ten minutes, occasionally a secondary rise or fall occurred. Since the experiments were usually terminated within three hours, the duration of these secondary changes cannot be stated.

In 2 instances the initial immediate rise in arterial pressure occurring at five seconds was followed by a fall at seven to eight seconds and a brief secondary rise before the definitive drop began. Both these animals showed prominent Traube-Hering waves in the control period.

The tendency of the diastolic pressure to drop more than the systolic was consistent. In one experiment the systolic pressure showed very little change throughout.

Electrocardiogram. The great majority of dogs showed changes in the electrocardiogram. Transient increase in amplitude of QRS in leads two and three occurred within a second or two of the injection. Occasionally T2 and T3 increased in amplitude at this time. Characteristically, within five to ten seconds the T waves in leads two and three showed progressive changes—flattening, splitting or inversion,

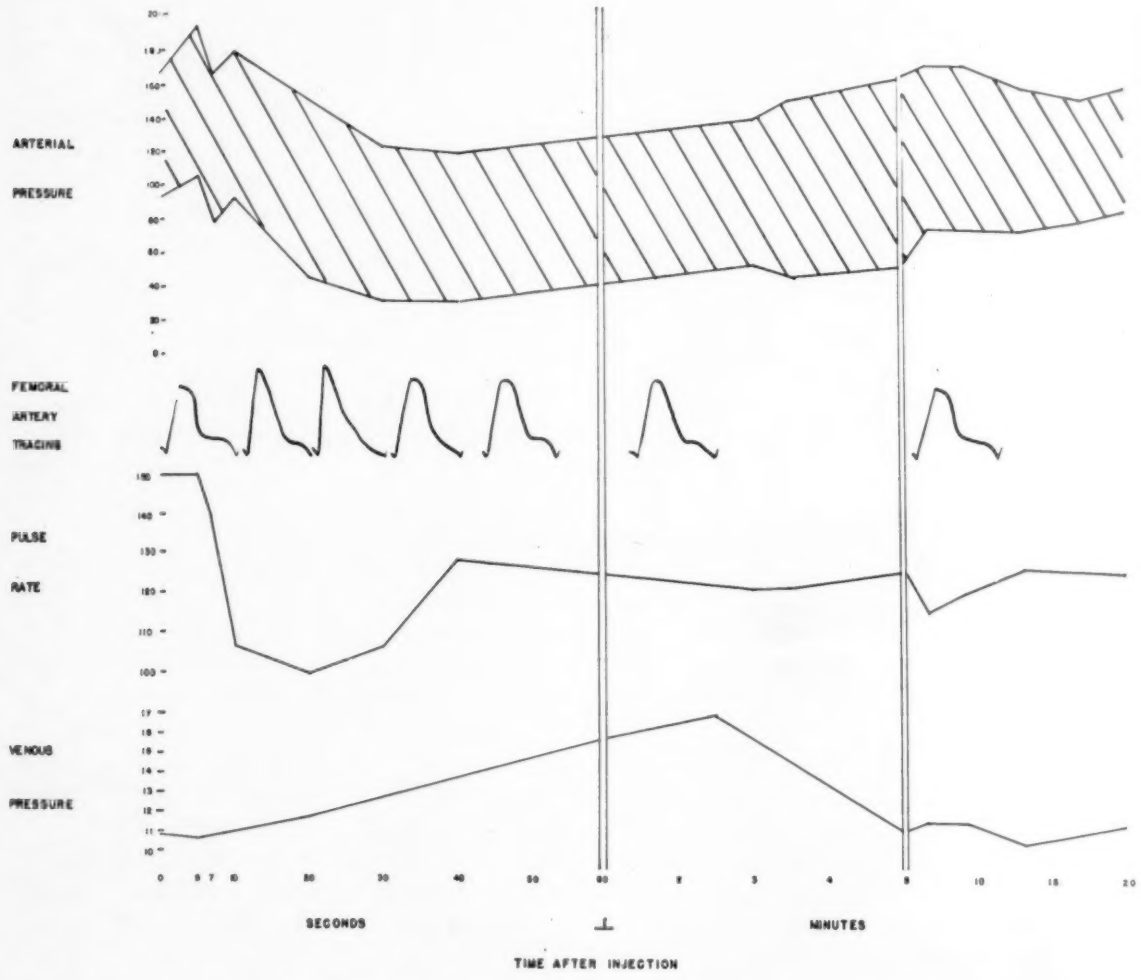

FIG. 2. The diodrast reaction in dogs. In this case the drop in diastolic pressure persisted longer than usual.

sometimes accompanied by depression of the ST interval. No disturbances of rhythm occurred from diodrast alone.

Heart Rate. The heart rate dropped 15 to 45 per cent. A distinct tendency was noted for the slowing to be more pronounced when the initial rate was most rapid. The heart rate usually began to drop ten seconds after the beginning of the injection, reached its lowest point at thirty seconds, remained at this level for thirty more seconds, then gradually returned to the initial level. In several cases, bradycardia of moderate degree persisted throughout the experiment.

Arterial Pulse Contour. At the height of the diodrast effect, the femoral pulse showed a more rapid rise, absence of rounding of the apex of the curve, more rapid fall, loss of the dicrotic wave, and increase in the height of the wave itself (Fig. 1). In 2 cases, pulsus alternans occurred, without corresponding changes in the electrocardiogram. This was a late occurrence, coming on ten minutes after the injection in one dog, and between five and eight minutes after it in the other. In the first animal, the pulsus alternans disappeared after a second injection of diodrast combined with epinephrine. The second animal was watched for one hour with continuation of the pulsus alternans during this period. By the next day the pulse was normal.

Effect of Dosage, Concentration and Speed of Injection. When 10 cc. of a 70 per cent solution or 20 cc. of a 35 per cent solution of diodrast was given as rapidly as possible, the effect was usually identical to that described above although occasionally the drop in pulse rate and blood pressure was not as marked. However, the same dosage, when given more slowly, had a much less pronounced effect. For instance, when 20 cc. of 35 per cent solution was given over a three minute period, all the usual effects occurred, but they developed more slowly, were not as pronounced, and lasted longer. One cubic centimeter of 70 per cent diodrast had no effect at all.

Effects of Repetition. No differences in the reaction to diodrast were noted when the same animal was given a second injection on the same day, after the effects of the original injection had worn off. In no case was a second injection given when the reaction to the first was still evident. When dogs were given a total of 60 cc. or more of 70 per cent diodrast during the course of one experiment (i.e., over a period of three hours) they usually died within twenty-four hours. Unfortunately, most of the dogs who died had also received other drugs, so that evaluation of the cause of death was difficult. Postmortem examinations of these animals showed nothing of significance. In several instances, the same dog was given injections about a month apart. The reactions were always characteristic; no evidence of sensitization to the drug was forthcoming.

Effects of Glucose, Saline and Gelatin. In order to evaluate the role played by hypertonicity, viscosity, amount of fluid and speed of injection, the following experiments were performed:

Saline: When 20 cc. of normal saline was given intravenously as rapidly as possible, the only effect recorded was an increase in the amplitude of T2 and T3 in one of the animals. The same amount of 5 per cent saline led to a slight rise followed by a slight fall of mean pressure, and minimal changes in T2 and T3 similar to those after diodrast. One animal which was given 20 cc. of saturated saline rapidly, immediately developed a bizarre arrhythmia and died within a few seconds.

Glucose: When 20 cc. of 50 per cent glucose solution was injected as rapidly as possible, the following changes were noted: An almost immediate increase in amplitude of T2 and T3 occurred. Within four seconds sinus bradycardia, followed by sinus arrest and sino-auricular block, were recorded. There was a rapid drop in systolic and diastolic arterial pressures, a rise in venous pressure, and progressive changes in the femoral pulse curve consisting mainly of increase in height of the curve without

loss of the dicrotic wave. The drop in arterial pressure was noted earlier, and the animal recovered sooner, than after diodrast, the systolic pressure returning to normal much more quickly than the diastolic. After atropine or bilateral vagotomy, slowing of the heart did not occur and the drop in arterial pressure was not as marked, although the electrocardiographic changes were again found.

Twenty cubic centimeters of 50 per cent glucose, given over a three minute period, caused a distinct elevation of both systolic and diastolic pressures, slowing of the pulse, and a rise in venous pressure, all maximum at two minutes. There followed a drop in arterial and venous pressures, below the initial level, persisting for at least fifteen minutes. No changes were noted in the arterial pulse contour. No electrocardiographic changes occurred.

Gelatin: Ten per cent gelatin served as a relatively inert substance of about the same viscosity as 70 per cent diodrast. When 20 cc. of 10 per cent gelatin solution was given rapidly to a dog, there followed a slight rise in systolic, diastolic and pulse pressures, maximum at seven and one-half seconds, followed by a distinct although slight fall, with the lowest point at fifteen seconds. No change in pulse rate was recorded. At two seconds the electrocardiogram manifested a slight increase in T2 and T3, followed in five seconds by slight increase in amplitude of QRS 2 and 3. The reaction to gelatin was the same after preliminary bilateral vagotomy.

Attempts to Modify the Diodrast Reaction. In order to eliminate the possibility that splanchnic vasodilatation was playing a major role in the depression of blood pressure, abdominal compression was applied to one animal during the injection of diodrast. The effect was unaltered.

Epinephrine: When a large dose of epinephrine was given, and diodrast injected after the epinephrine effect had worn off, as manifested by return of blood pressure and pulse rate to normal, the usual diodrast effects occurred.

Several animals were given epinephrine and diodrast in the same syringe. When large doses of epinephrine were given in this way (i.e., 0.1 to 1 mg.) typical and marked epinephrine effects were noted in blood pressure, pulse contour, and heart rate, and the diodrast reaction was completely obscured. With smaller doses of epinephrine, however (0.01 to 0.02 mg.) and the same standard amount of diodrast, the epinephrine effect occurred first. There followed a drop in arterial pressure which was not as marked as was usually seen with diodrast alone, occurred slightly later, and had a tendency to persist longer. Indeed, in one instance, the blood pressure dropped progressively to shock levels, and the dog had to be revived with oxygen and intravenous fluids. (This particular animal, however, had already received two previous injections of 10 cc. each of 70 per cent diodrast, one combined with epinephrine. In addition, this dog had developed pulsus alternans following the first diodrast injection.)

In order to prevent a considerable part of the diodrast reaction, sufficient epinephrine had to be given first to raise the arterial pressure to dangerous levels. In short, the two drugs did not seem to counteract each other, but rather exerted their effects at different times, depending on their comparative concentrations.

Ephedrine: This drug was given in the same syringe with the diodrast. When a very large dose of ephedrine sulphate (10 mg.) was given, the diodrast effect was manifested only by a slight drop in systolic and diastolic pressures from ten to thirty seconds after the injection, to be followed by the typical ephedrine response. The only difference between this drug and epinephrine was its slower onset of action, which permitted the early diodrast effect to become manifest.

Paredrine: Ten milligrams of paredrine hydrobromide was given in the same syringe with 20 cc. of 70 per cent diodrast. Both a lowering of the arterial pressure, and a slowing of the heart occurred, to-

gether with changes in the pulse wave contour, as seen following diodrast. However, these changes lasted only fifty seconds and were followed by a prolonged and marked blood pressure rise, attaining a maximum at 140 seconds and persisting for twenty minutes. A late tachycardia also occurred. (Twenty minutes after the injection of paredrine and diodrast in this dog, another injection of diodrast caused a rise in systolic and diastolic pressures, which, after a minute, gave way to a progressive fall in pressures terminating in death at four and one-half minutes. However, this animal received a total of 60 cc. of 70 per cent diodrast and it is difficult to draw any conclusions.) Paredrine hydrobromide, when given by mouth, had no effect on the diodrast reaction.

Neosynephrine: One animal, previously completely atropinized, was injected with 0.5 mg. of neosynephrine hydrochloride. In one minute, at the height of the blood pressure rise, 20 cc. of 70 per cent diodrast was injected. The result was a typical diodrast reaction in every way.

Pitressin: When diodrast was given at the height of the pressor effect of 0.2 cc. of pitressin (20 pressor units per cc.) the usual diodrast effect occurred. When the same dose of pitressin was given in the same syringe with the diodrast, the pitressin effect was not evident; the diodrast effect was typical in every way.

Atropine: Atropine sulfate in large doses, given a considerable interval before the diodrast, failed to affect the arterial pressures, pulse rate or electrocardiographic changes of the diodrast reaction.

Vagotomy: In several animals, bilateral vagotomy was performed in the following manner: One vagus was cut above the bifurcation of the carotid artery; the proximal end was stimulated; if no reaction occurred, the other vagus was cut in the same way. After equilibrium was restored (usually twenty to thirty minutes) the diodrast injection was given. Although minor differences occurred in the reactions of these animals as compared with controls, these differences showed no distinct trend and were probably not significant. (All the animals whose vagi were cut, died within twenty-four hours, usually from bronchopneumonia.)

Tetraethylammonium: Tetraethylammonium chloride (etamon, Parke, Davis and Co.) in a dose of 100 mg. intravenously, caused a distinct drop in arterial pressure, very slight cardiac slowing, and changes in the arterial wave contour of a different character from those seen following diodrast. When diodrast was given to this animal after the peak effect of tetraethylammonium had been reached and begun to subside (three minutes) the following took place: (1) The arterial pressures, which had already dropped considerably, dropped further, to approximately the same point observed in the same animal previously, with diodrast alone. (2) The pulse pressure was not as great as in the control. (3) Very little further slowing of the heart occurred. (4) No electrocardiographic changes took place, whereas marked changes occurred in the control.

Histamine Antagonist: Twenty-five milligrams of phenargan (R. P. No. 3277) one of a new series of potent antihistamine drugs, given in the same syringe with the diodrast, failed to alter the reaction.

Interpretation of Results: Effects on Peripheral Vessels. That diodrast is a potent vasodilating agent is attested to by the fall in blood pressure and the changes in the arterial pulse contour. The diodrast reaction, particularly in humans[9] is suggestive of a parasympathetic discharge such as would occur, for example, after the administration of acetyl-beta-methyl choline. These effects are a drop in blood pressure, bradycardia, nausea, flushing of the skin, cough, dyspnea and sweating. However, the inability of atropine, vagotomy, and tetraethylammonium to prevent the cardiovascular reaction in dogs indicates that the peripheral effects are probably exerted directly on the smooth muscle of the vessel walls. A direct action on the peripheral vessels is also suggested by the increase in

permeability of cerebral vessels noted by Broman and Olsson.[1]

The effects of sympathomimetic drugs depend to a large extent on the rapidity of onset and duration of their action compared to that of diodrast. In these respects, epinephrine most closely parallels diodrast and might, therefore, be considered a satisfactory antagonist. However, it obscures the diodrast reaction only when given in dangerously large doses. In smaller doses, the epinephrine effect occurs first; the vasodepressor action of diodrast is delayed or minimized. Our experiments tend to confirm the theoretical objection to the use of epinephrine to combat the vasodepressor type of diodrast reaction, namely, that the late depressor effects of epinephrine may potentiate, rather than combat, the fall in blood pressure. It is suggested that these results are of importance in the treatment of the diodrast reaction in humans.

The slower acting sympathomimetic drugs (ephedrine, paredrine, neosynephrine) were also ineffective in preventing the diodrast-induced fall in blood pressure. When these drugs were given at the same time as the diodrast, the depressor effect occurred first, followed by the sympathetic effects. In the one case where diodrast was given at the height of the effect from a sympathomimetic drug (neosynephrine), the usual diodrast reaction occurred.

Our experiments indicate that diodrast is capable of reversing and preventing the vasoconstrictor effects of pitressin. These results are at variance with those of Kraus[6] who reported that a group of iodine-containing contrast media (including perabrodil (diodrast)) was not capable of preventing the vasoconstrictor effects of pituitrin or of "adrenalin bodies," nor of neutralizing the pituitrin action at its height. The discrepancy can probably be explained by the variations in amounts of the various drugs used.

Although a preliminary vasoconstriction has been observed repeatedly in perfusion experiments with diodrast,[2,4] the rise in arterial pressure which we observed occurred within two or three seconds, which we consider too soon to be on the basis of a vasoconstriction. Presumably the early rise in blood pressure is caused by a direct stimulation of the heart.

Effects on the Heart. Since it was unaffected by vagotomy and atropinization, the bradycardia which we observed regularly after diodrast injection is presumed to be a result of direct action on the heart muscle, following initial stimulation indicated by immediate rise in blood pressure. Electrocardiographic changes, nonspecific in character, are further evidences of influence on the myocardium. Even more striking evidence of prolonged myocardial depression is seen in the 2 cases of pulsus alternans. The ability of tetraethylammonium chloride to prevent the diodrast-induced electrocardiographic changes in one animal, is unexplained.

Effects on Venous Pressure. The reason for the rise in venous pressure, which usually paralleled the fall in arterial pressure, is not clear. One would expect that the peripheral vasodilatation would diminish the venous return to the heart, and lead to a reduction of pressure in the large veins, unless there was a coincidental reduction of cardiac output with consequent interference with the emptying of the right side of the heart. The introduction of a large amount of viscous fluid into the blood stream is another possible explanation. The rapid injection of 20 cc. of normal saline did not change the venous pressure. Injection of 50 per cent glucose raised it considerably, whether given slowly or rapidly. Unfortunately, the venous pressure was not determined in the animal receiving gelatin.

DISCUSSION

The use of diodrast for angiocardiography is a unique experience in medicine in that the object is to inject into the blood stream as large an amount of drug as pos-

sible, in the shortest possible time. In general, diodrast is a substance of low toxicity. It has been our desire, in these experiments, to evaluate not only the drug itself, but the relative roles played by the amount of fluid injected, its concentration, osmotic pressure and viscosity, and the speed of injection. Although incomplete, our experiments indicate that all of the above factors are involved in the typical diodrast reaction. Since normal saline injected in the same way as the diodrast has no effect whatever, the possibility can immediately be dismissed that the diodrast reaction is caused solely by the injection of a large amount of fluid rapidly. On the other hand, it has already been demonstrated that the severity of the reaction is a function of the speed and concentration. Fifty per cent glucose, a viscous, hypertonic solution, causes both a steep drop in arterial pressure and a slowing of the pulse, but the difference in arterial pulse contour as compared to diodrast, and the prevention of the bradycardia by atropine and vagotomy, indicate that different mechanisms are involved. Both 5 per cent saline and 10 per cent gelatin cause a rise followed by a fall in arterial pressures, related in time to the diodrast effect. The one thing that these two substances have in common with diodrast is an elevated osmotic pressure as related to blood plasma. (Interestingly enough, the immediate drop in arterial pressure when 50 per cent glucose was given rapidly, was replaced by a rise in pressure when the substance was given over a three minute period.) On the other hand, an initial rise in arterial pressure was lacking in the animals receiving 50 per cent glucose rapidly whether or not vagotomy or atropinization had been performed.

Five per cent saline gave rise to electrocardiographic changes similar to those following diodrast injection, while normal saline, glucose, and gelatin did not.

Many of these findings are difficult to evaluate but it can be stated with some assurance that the "diodrast reaction" is in part caused by the drug itself, in part by the nonspecific factors mentioned above.

SUMMARY

When given intravenously in 70 per cent solution, in large amounts and as quickly as possible, diodrast has the following effects on the intact dog anesthetized with nembutal: A rise followed by a fall of arterial pressure; a rise in pulse pressure associated with marked changes in the contour of the femoral pulse; a rise in venous pressure and a fall in the pulse rate; and changes in the electrocardiogram. These effects are characteristic and reproducible. The same results are obtained to a somewhat lesser degree with a 35 per cent solution.

This typical "diodrast reaction" can be modified by changes in the speed of injection but is not completely eliminated even when the injection is given very slowly.

The most significant of the diodrast actions is vasodilatation. Stimulation followed by depression of the cardiac muscle also occurs. In two dogs, pulsus alternans was noted.

Efforts to prevent the vasodepression failed. These included abdominal compression, sympathomimetic drugs, a vasoconstrictor (pitressin), parasympathetic blocking agents (atropine, vagotomy), an autonomic blocking agent (tetraethylammonium), and an antihistaminic. Evidence was obtained suggesting that the secondary vasodepressor action of epinephrine may potentiate that produced by diodrast.

No evidence of allergic sensitization occurred in dogs which received two injections of diodrast several weeks apart.

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IN VIVO LOCALIZATION OF RADIOACTIVE SILVER AT PREDETERMINED SITES IN TISSUES

PRELIMINARY REPORT

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NASHVILLE, TENNESSEE

THE availability of a long half-life silver ($Ag^{108,110}$, 225 days) makes possible the study of its distribution in the animal body. Its use becomes more practical for this purpose than the short half-life isotope (Ag^{111}, 7.5 days) because experiments can be carried out over relatively long periods. On the other hand, the short half-life isotope may prove to be valuable in tumor therapy in humans provided it can be localized at or near the site of the lesion in sufficient concentration.

Preliminary experiments along several lines have been carried out in these laboratories with results of sufficient interest to be reported.

EXPERIMENTAL

The cultures used in this study were two strains of *Staphylococcus aureus* recently isolated from carbuncles. All injections were made from a proteose peptone broth culture which had been incubated at 37° C. for sixteen hours. In one experiment 3 adult albino rats were given an intradermal injection of 0.1 milliliter of the organism in the right hind leg. Forty-eight hours later these 3 rats were given an injection at the same site of 2 milliliters of a solution of $Ag^{108,110}NO_3$. An additional 3 rats were given a similar injection of radiosilver nitrate in the right hind leg and served as controls. Seventy-two hours after injection of radioactive silver, the animals were sacrificed, and the right hind legs, hearts, and lungs were subjected to a wet ashing procedure.

The organs were placed in Kjeldahl flasks and 20 to 50 milliliters of concentrated H_2SO_4, together with several crystals of $CuSO_4$, were added. The mixtures were heated until digestion was complete, more acid being added if necessary. The digests were diluted after cooling by careful addition of 150 milliliters of distilled water and 5 milliliters of a solution of ordinary silver nitrate containing 5 milligrams per milliliter was added to act as carrier silver. The silver was then precipitated in small beakers by adding 10 per cent NaCl. The precipitates were allowed to settle overnight and the supernatant fluid was removed as completely as possible by suction. The precipitates were then removed from the beakers with the aid of a policeman and a little water and placed into specially constructed tubes. The latter were made by cementing glass cylinders with the aid of plastic to the inside of small metal salve boxes used as containers for radioactive samples to be counted under the Geiger-Müller tube. The precipitates were allowed to settle and after removal of the supernatant fluid they were left to dry at room temperature. The glass cylinders were then carefully removed and the activity of the sample was determined with the Geiger-Müller counter.

In a second experiment 9 animals were used. Three again served as controls with injections of 2 milliliters of radiosilver nitrate in the right hind legs, 3 served as experimental animals and as before received injections of the organism and the $Ag^{108,110}NO_3$ in the right hind leg, and the last 3 were injected with the suspension of *Staphylococcus aureus* in the right hind leg but with the radiosilver nitrate in the left hind leg. The last 3 animals were, as is seen below, to serve as a crucial test of the phenomenon being studied.

In the case of rat No. 6 in the first experiment an obvious infection of the skin near the left shoulder was observed. The infected tissues were removed and treated as described above for the other organs.

RESULTS OF THE EXPERIMENTS

It is clear from Tables 1 and 11 that as much as 10 per cent of the activity may remain in the leg injected with $Ag^{108,110}$ after seventy-two hours. This is of interest since it gives some idea of the rate at which

the injected isotope is removed from the site of injection. The average count for the control legs (right leg injected, no infection) is 206.6 counts per minutes for experiment I and 147.6 counts per minutes for experiment II, the average for 6 animals being 177.1 When the injection of $Ag^{108,110}$ was carried out together with that of *Staphylococcus aureus* in the same leg, the count In the infected leg (not injected with radiosilver) the count approached that seen when a leg was injected with $Ag^{108,110}$ and *Staphylococcus aureus* (average 397 counts per minute).

TABLE I

Rat No.	Type and Site of Injection		Activity,* Counts per Minute			
	Right Hind Leg	Left Hind Leg	Lung	Heart	Right Hind Leg	Left Hind Leg
1	Radiosilver	—	29	—†	229	—
2	Radiosilver	—	7	469	222	—
3	Radiosilver	—	0	6	169	—
4	Radiosilver					
	Staph. aureus	—	0	0	1,390	—
5	Radiosilver					
	Staph. aureus	—	0	0	925	—
6‡	Radiosilver					
	Staph. aureus	—	0	4	861	—

* Control sample treated by the ashing procedure for animals No. 1 to 6: 2,480 counts per minute.
† Lost during ashing.
‡ In rat No. 6 an obviously infected area in the skin was dissected out and carried through the ashing procedure. The count was 253 counts per minute.

DISCUSSION

Much remains to be learned concerning the distribution of silver in various organs of the animal body following its introduction into open lesions and its administration by other routes. Muller[8] has published evidence indicating that an oily dispersion of anhydrous silver oxide containing 5 per cent silver oxide will yield its entire silver oxide content to the animal system by simple inunction on the surface of the skin or by application to open lesions or mucous surfaces and that when so absorbed, silver in some form or other can be readily found in both urine and feces of the treated animal. The analysis of the skin and underlying tissues of animals treated by inunction failed to show any signs of deposits of silver or any compounds of this metal so that complete systemic distribution of the administered oxide is more probable. Win,[15] many years ago, injected silver granules into the skin of rabbits, but was unable to demonstrate any permanent disposition of the metal by removal of a piece of skin

after seventy-two hours in the leg was increased five fold in experiment I where the average was 1,058.6 counts per minute and two and one-half fold in experiment I where the average was 373.3 counts per minute. The marked increase in activity found in the presence of the induced infection seemed unlikely to be due to chance. Apparently some mechanism for inhibiting removal of the radioactive silver from the injected leg was operating or, what is even more likely, $Ag^{108,110}$ was being transported back to the site of infection. The results with animals No. 13, 14, and 15, experiment II, seem to indicate that the latter possibility was more plausible. In these animals the radiosilver was injected into the left hind leg while the infection was set up in the right hind leg. Only a small amount of activity remained in the leg injected with $Ag^{108,110}$ (average 32 counts per minute).

six weeks after injection. Jacobi[5] was unable to produce generalized argyria by subcutaneous injections of silver solution in rabbits. Pincussen and Roman[9] injected silver sulfate subcutaneously into rats and demonstrated silver in the blood, skin, kidney, spleen and liver. In this laboratory by use of $Ag^{108,110}$ as a tracer the metal has been demonstrated following subcutaneous injection in heart, lung, liver, spleen, kidneys, testes, ovaries, feces, and a number of the larger muscles of the albino rat.[14] Apparently the subcutaneous injection of soluble silver salt is followed by its complete distribution throughout the animal body.

Concerning the mode of transport of silver in the animal body, investigators are in general agreement that silver has a marked affinity for the vascular tree.[2] Blumberg and Carey[1] in a human case of generalized argyria concluded that the major part of silver was in the plasma and found only a small portion in the cell fraction. Minz[7] added a silver salt to blood and could demonstrate the presence of the metal in the plasma but not in the cells. Silver granules have been found on dark field examination of leukocytes[12] and it appears certain that silver may be transported by phagocytic cells.[4] In a number of cases following absorption of silver by various routes, considerable amounts of silver have been demonstrated in the phagocytic cells of the spleen and lymph nodes. The metal has also been found in histiocytes.

Hahn and colleagues have found that radioactive colloidal manganese localizes in the pancreas while radioactive colloidal gold localizes in the reticulo-endothelial system.[10] McClintock and Friedman[6] have utilized the specificity of the union of antibody with antigen for localization of dyes and metals in the tissues. In this case the dye or metal concerned was first combined with purified antibody. The dye- or metal-antibody combination was injected into the left femoral vein after the specific antigen was injected into the leg muscle. A roentgenogram showed depositions of the metal (uranium) at the site of injection of the antigen.

In the present experiments it is believed that the localization of radiosilver is due to combination of the metal with the leukocytes for transport and concentration of the active metal in an infected area due to the well known phenomenon of phagocytosis.

Table II

Rat No.	Type and Site of Injection		Activity,* Counts per Minute			
	Right Hind Leg	Left Hind Leg	Lung	Heart	Right Hind Leg	Left Hind Leg
7	Radiosilver	—	9	18	73	—
8	Radiosilver	—	0	21	50	—
9	Radiosilver	—	10	0	320	—
10	Radiosilver					
	Staph. aureus	—	8	9	176	—
11	Radiosilver					
	Staph. aureus	—	287	13	456	—
12	Radiosilver					
	Staph. aureus	—	6	0	488	—
13	*Staph. aureus*	Radiosilver	8	2	213	37
14	*Staph. aureus*	Radiosilver	16	14	573	37
15	*Staph. aureus*	Radiosilver	6	15	405	22

* Control sample treated by the ashing procedure for animals No. 7 to 15: 2,496 counts per minute.

SUMMARY

1. Radiosilver has been localized at a predetermined site in an animal tissue.

2. The active metal concentrates in areas of spontaneous or induced infection.

3. A possible explanation of the phenomenon consists in the theory that the silver, being transported by white blood cells concentrates in the areas as a result of phagocytosis.

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DEPARTMENT OF TECHNIQUE

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A METHOD FOR IMPROVING ROENTGENOGRAMS OF THE COLON AFTER COLOSTOMY

By WILLIAM M. LOEHR, M.D.
INDIANAPOLIS, INDIANA

THE roentgen examination of the colon by barium enema in patients with a colostomy has always presented one major difficulty and inconvenience to the radiologist and the technician. It has always been difficult to obtain roentgenograms of excellent quality because of the interference and obtrusion caused by the catheter or other tube inserted into the colostomy opening to deliver the barium solution. At the time the films are to be exposed the enema tubing becomes a nuisance and the technician may elect to do one of two things: (*a*) make the exposure with the tube held in the colostomy opening and the patient *supine*, with consequent loss of detail and sharpness of the colon image due to not having the patient prone, (*b*) remove the enema tubing and cover the colostomy opening with a gauze compress or other dressing and make the exposure with the patient *prone*, with consequent interfering shadow of the compress material and invariable soiling of the roentgenographic table as barium leaks out the colostomy producing ugly barium rivulets on the finished roentgenogram.

The most satisfactory solution to this problem if neatness and clarity in the finished roentgenograms are desired is presented here. At the conclusion of the roentgenoscopic observations the radiologist removes the enema tubing slowly and gently, at the same time inserting a rubber nursing nipple (Fig. 1) of a type and make* available at any drugstore. The patient holds it in place with the fingers while turning into the prone position and removes the fingers from the flat surface or base of the nipple when the technician has completed the centering and positioning

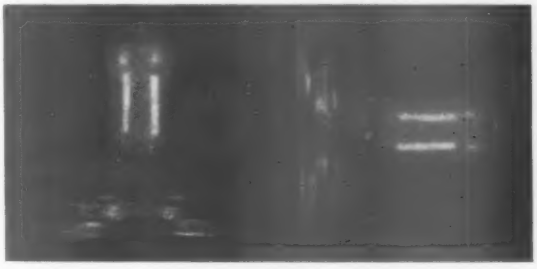

Fig. 1

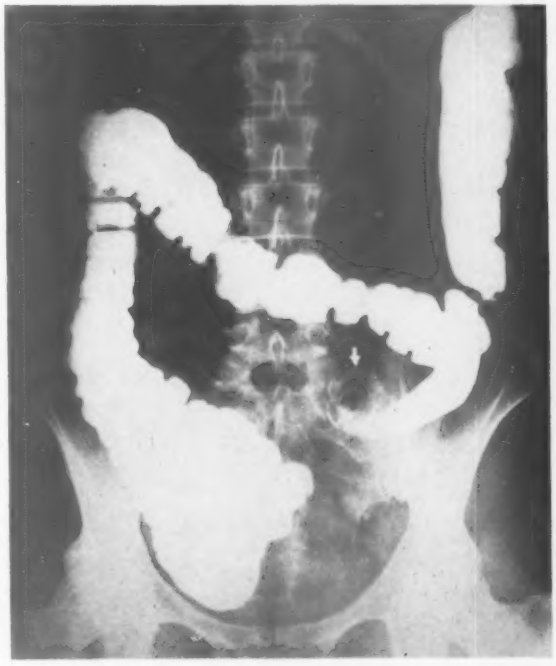

Fig. 2

* Steadifeed Nursing Nipple, Searer Rubber Co., Akron, Ohio.

of the patient on the table. The resulting roentgenogram is shown in Figure 2. The patient holds the nipple in place again after the exposure and removes the nipple when in position to evacuate the enema. After evacuation the nipple is replaced in the colostomy opening for the evacuation film (Fig. 3). In our experience but one size of nipple has been required for patients of varying ages and size.

Fig. 3

A few of the advantages of the nipple may be listed: (1) It is practically non-opaque. (2) It extends a short way down the colostomy making an excellent plug, and the base of the nipple (the portion intended for connection with the nursing bottle) is perfectly flat and thin, thus coming into perfect apposition with the roentgenographic table when the patient is *prone*. This is not possible with other convenient articles which might be used in like manner such as the rubber bulb of an Asepto syringe, etc. (3) As a result of (1) and (2), very often peristaltic movement will produce movement in the distal portion of the nipple while it is in place and produce just enough motion of the nipple during exposure of the film to practically eliminate the faint image of the nipple on the finished film (Fig. 3). This is analogous to the disappearance of faintly calcified fetal structures on a roentgenogram when these structures were in motion during the making of an obstetrical roentgenogram.

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Thirty-Third Annual Meeting: Atlantic City, N. J., 1951.

EDITORIALS

THE FIFTY-FIRST ANNUAL MEETING OF THE AMERICAN ROENTGEN RAY SOCIETY

(FIFTIETH ANNIVERSARY MEETING)

THE week of September 26–29, 1950, the American Roentgen Ray Society celebrated in St. Louis, Missouri, the Golden Anniversary of its founding. This occasion was commemorated not only by a program of superlative quality but by the issuance of a brochure commemorating the organization of the Roentgen Society of the United States in St. Louis, Missouri, in March, 1900. The Roentgen Society of the United States subsequently became known as the American Roentgen Ray Society.

The beautiful brochure commemorating the Fiftieth Anniversary of the founding of the Society was a product of the Committee on Local Arrangements under the chairmanship of Dr. Wendell G. Scott. In a preface to this brochure Dr. Scott and his committee express their gratitude and appreciation to Dr. E. H. Skinner, Dr. G. E. Pfahler, Dr. A. C. Christie and Dr. Otto Glasser whose contributions and interest in the brochure make it such a splendid souvenir of the occasion.

The meeting was called to order on Tuesday morning at eleven o'clock by President U. V. Portmann, following which he made the presentation of Scientific Awards given at the 1949 meeting. Dr. Armond D. Fries, President of the St. Louis Medical Society then welcomed the American Roentgen Ray Society to St. Louis for the celebration of its Golden Jubilee Meeting. Dr. Fries said among other things that St. Louis was proud of many of its fine contributions not only to medicine but to the arts and sciences as well but that they were particularly proud to claim their city as the founding city of the American Roentgen Ray Society. Dr. Bernard P. Widmann was then installed as President of the Society by Dr. M. J. Geyman, the Chairman of the Executive Council. The subject of Dr. Widmann's presidential address, "The Triumphs of Palliation in Radiation Therapy," was one on which he is very competent to speak. Following this Dr. Edward H. Skinner gave a delightful talk on "Fifty Years Ago—The Birth of the American Roentgen Ray Society" which is an elaboration of his historical essay in the commemorative brochure. Following Dr. Skinner's excellent talk, Dr. George E. Pfahler discussed "Fifty Years of Trials and Tribulations in Radiology," years through which he himself had passed, a lifetime given to professional radiology which places him in the forefront of radiologists in the world. After Dr. Pfahler's historical discussion, Dr. Arthur C. Christie gave a very stimulating and inspiring talk on "Fifty Years of Progress in Radiology," and no one stands in a better position to survey the fifty years of progress in radiology than does Dr. Christie because he has been in the very vanguard of progress in the medical and radiological world throughout these many years.

Dr. Christie called attention to the fact that we were not only celebrating fifty years of progress in radiology but were utilizing this opportunity to take stock and to look into the future and "If we are to receive the full impact and inspiration of

this celebration we must consider seriously the price which has been paid for the progress so far achieved; it is a measure of the price which must be paid for future progress. The past and the future are inseparable. Progress during the past 50 years would have been impossible except for achievements prior to that time. The discovery of the x-ray and of radioactivity would have been long delayed had it not been for the work of Faraday, Maxwell, Crookes, Plücker, Hittorf, Hertz, Lenard, and many others. In like manner," so Dr. Christie said, "the 50 years which we now celebrate constitute the foundation for the progress of the future." In a brilliant discussion he sketched briefly the progress that radiology has made and the backgrounds for such progress. Toward the end of his discussion he called attention to a most important fact when he said, "No dangers threaten us from without which cannot be met if our own house is in order. Internal decay is always a more potent cause of collapse than external pressure. . . . Our problems now are different but not more difficult than those of 50 years ago. Among the radiologists of this day are the pioneers who will lead in the progress of the next 50 years. We can wish for them nothing more fitting than that they may be endowed with a great measure of the faith and courage and confidence in the possibility of progress which characterized the pioneers of 50 years ago."

Thus was set the stage for the excellent scientific program which was to follow. Dr. Widmann and his Program Committee had arranged a series of papers and discussions which have not been surpassed at any of the former meetings of the Society. The program was a well balanced one having to do with therapeutic measures including chemotherapy, radioisotopes, roentgen therapy and radium therapy; diagnostic procedures of various types dealing with the roentgen ray and radioisotopes and the newer fields of exploration concerned with arteriography. One of the most important symposiums presented at the meeting was one on the subject of "The Training of Residents in Radiology." This symposium was opened with a competent discussion by Dr. B. R. Kirklin in which he called attention to the trend in radiology and also the desires of some as to how radiology should be practiced in the future. This symposium dealt also with the training of residents in diagnosis; training in therapy, and training in physics, so the whole field of the present trend in the teaching of radiology was adequately covered.

As always, the Caldwell Lecture, which was given on Wednesday evening, was one of the high points of the meeting. This was delivered by Dr. Henry L. Bockus, Professor and Chairman of the Department of Internal Medicine, Graduate School of Medicine, University of Pennsylvania, Philadelphia. He chose for his topic "The Role of Roentgenology in Gastroenterology." He gave a most stimulating talk dealing not only with our present knowledge of gastroenterological problems which the roentgen-ray studies have helped to elucidate but pointing out in a provocative manner some problems of investigation which the radiologist and the gastroenterologist might pursue in the too little known so-called neuroses which manifest themselves in gastric and intestinal disturbances.

Many of the papers that were presented in the scientific section were amplified and extended in the Scientific Exhibit, and in addition there were numerous other excellent exhibits, and the Scientific Exhibit Committee under the chairmanship of Dr. R. A. Arens is to be congratulated upon securing such a beautiful and instructive group of exhibits, probably one of the best that the Society has gathered together. A detailed description of the scientific exhibits and the awards given appears elsewhere in this issue of the JOURNAL.

The Commercial Exhibit, which is always an instructive feature of the meeting, was an extensive one and the exhibits were most attractively arranged and presented,

and many of the exhibits had displays which were of interest in connection with the Fiftieth Anniversary of the Society.

The Instructional Courses which are so ably arranged by Dr. Harry M. Weber again attracted capacity audiences and much enthusiasm was shown for the Faculty which had been chosen and the subjects presented.

The social aspects of the meeting were in no way neglected and were all that might be desired in a city so hospitable as St. Louis. The Annual Golf Tournament was held on Monday at the Sunset Country Club, with the annual golf dinner in the evening. The banquet on Thursday evening was well attended and the decorations carried out the Golden Anniversary theme in a most attractive manner. The Ladies Committee under the chairmanship of Mrs. Wendell G. Scott had provided adequate entertainment for the ladies, consisting of trips to numerous points of interest in St. Louis as well as a Golf Widows Dinner on Monday evening, and several luncheons.

In spite of the fact that this annual meeting of the Society came so quickly upon the heels of the International Congress held in London, there was a large attendance, the total registration being over twelve hundred.

The Society desires to express its appreciation to the Convention Bureau of St. Louis and to the management and personnel of the Hotel Jefferson for the fine manner in which they contributed toward the success of the meeting and we would be greatly remiss in our acknowledgments if we did not again express our great thanks to the Local Committee of Arrangements for the splendid manner in which they contributed to the pleasure and profit of the meeting.

As this issue goes to press, word has been received of the death of Dr. Percy Brown at the age of seventy-four at his home in Egypt, Massachusetts, on October 8, 1950. Dr. Brown was a pioneer radiologist who was internationally known in his field. An account of his life and work will appear in an early issue of the Journal.

ROBERT HERVEY LAFFERTY
1878–1950

ROBERT HERVEY LAFFERTY died of acute leukemia in Charlotte, North Carolina, July 31, 1950 at the age of seventy-two, having been confined to bed less than two weeks.

Dr. Lafferty was born in Davidson, North Carolina, on August 28, 1878, the son of James Stewart Lafferty, M.D., a country doctor, and Hattie Kerns Lafferty. After receiving his A.B. and M.A. degree in Chemistry from Davidson College, he taught in the schools of North Carolina and Florida for several years. He received his medical degree from the North Carolina Medical College and followed this with post-graduate work at the University of Chicago. He served as registrar and professor of chemistry and physiology at his Alma Mater for several years.

Dr. Lafferty began private practice in 1915, specializing in urology and radiology, and two years later he confined his practice to radiology. During World War I, he did all of the roentgenological work for Camp Greene, a camp of 65,000 men, in his office. In 1918 he was joined by Dr. Clyde C. Phillips, who died in 1939, and in 1937 Dr. O. D. Baxter became associated with Drs. Lafferty and Phillips. At the time of his death the group was composed of Dr. Robert H. Lafferty, Dr. O. D. Baxter, Dr. James B. Hall, and Dr. John O. Lafferty, his younger son.

Dr. Lafferty was a member of the Mecklenburg County Medical Society, North Carolina Medical Society, Southern Medical Association, Fellow of the American Medical Association, American Roentgen Ray Society, and Radiological Society of North America, having served as vice-president and as a member of the Executive Committee. He was a charter member and Fellow of the American College of Radiology. He was one of a group that organized the Section on Radiology of the Southern Medical Association.

Dr. Lafferty was very active in religious and civic affairs of Charlotte. He was for thirty years superintendent of the Sunday School of the Second Presbyterian Church, and served as an elder in that church for many years. He had been a director of the Charlotte Y.M.C.A. and was on the local executive council of the Boy Scouts of America. For years he was interested in horticulture, and grew some of the finest iris this section of the country has ever seen, until forced to give up this work because of irradiation dermatitis of his hands, a product of his early work before the elements of protection were well understood.

Robert Hervey Lafferty

He had written many papers and recently had published a History of the North Carolina Medical College, and at the time of his death was working on a History of the Second Presbyterian Church of Charlotte.

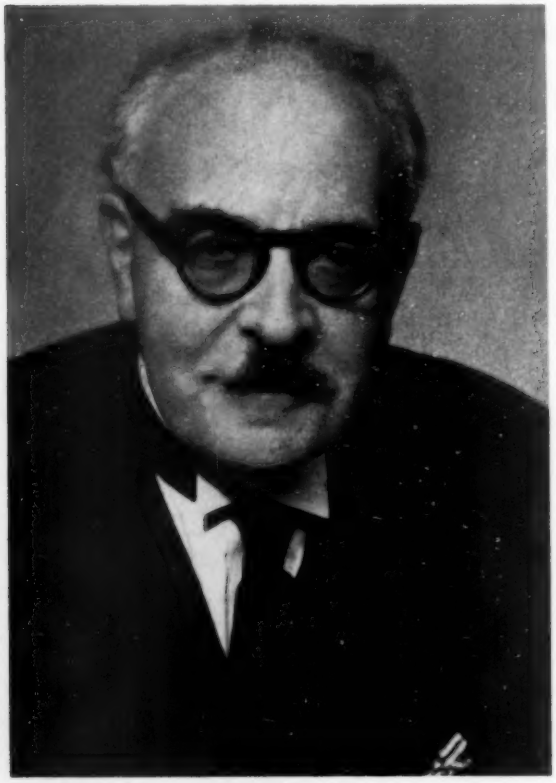
He is survived by his wife, the former Edith K. Fry, and two sons, Dr. R. H. Lafferty, Jr. of Oak Ridge, Tennessee, and Dr. John O. Lafferty, who has been associated with his group since January, 1949.

Dr. Lafferty will be missed by an unusually large number of close friends and particularly by his associates. We all feel, however, that we are better doctors and men for having known him and having been associated with him.

O. D. Baxter, M.D.

ALFRED ROSSELET
1887–1950

DR. ALFRED ROSSELET, one of the eminent radiologists of Europe, passed away (postoperatively) on March 22, 1950, in the Saint-Loup Hospital, near Lausanne, Switzerland. A man of a broad cultural, scientific and clinical knowledge and training, he distinguished himself as an outstanding professor.



Alfred Rosselet

Born at Neuchâtel on August 9, 1887, he grew up at nearby Couvet, his father being the pastor of that beautiful Swiss town in the Jura Mountains. He studied at the Gymnase Scientifique of Lausanne and then at the Faculty of Sciences of the University of Lausanne. In 1909 he was granted the degree of "Doctor of Physical and Natural Sciences" on the approval of his thesis: "Recherches sur les phenomènes actino-electriques et leurs relations avec l'ionisation de l'air." From 1909 to 1910 he studied in Paris, taking courses given by such physicists as Langevin, Madame Curie and Becquerel.

On his return to Lausanne he taught physics at the Gymnase Scientifique and at l'Ecole Normale for a year. At the age of twenty-four he decided to study medicine. He immediately started at the University of Berne. He continued his medical studies and training at the University of Geneva and on the presentation of his thesis "Contribution à l'étude du volvulus de l'estomac" he was granted the federal diploma and degree of "Doctor in Medicine."

For a year, in 1916, he served as a physician to the French soldiers interned in Switzerland. From 1917 to 1920 he directed the department of radiology at

l'Hôpital de Geneve (Geneva). From 1920 to 1922 he was the medical and scientific assistant of Professor A. Rollier at Leysin Sanatoria, Switzerland. During these years he accomplished significant research pertaining to heliotherapy, role of epidermic pigment, chlorophyll and ultraviolet rays.

In 1922 he was invited to direct the department of radiology at the university hospital of Lausanne (Hôpital Cantonal). A year later he was nominated "privatdocent." In 1926 he was installed as professor of medical radiology at the University of Lausanne, becoming thus the first person in Switzerland to secure a professorship in the new specialty.

With a few colleagues, in 1924 he founded the "Centre Anticancereux Romand" (Cancer Society of the French Speaking Part of Switzerland). From 1925–1936 he was the director of this society. In 1936 he was elected its president.

At various times he became the president of the Swiss Society of Natural Sciences and of the Cancer Society of Switzerland. From 1934 to 1937 he was president of the Swiss Society of Radiology. In 1928 he organized the first "International Conference on Light" which was held at Lausanne and at Leysin. In 1935 he was the Swiss delegate to the International Congress of Radiology at Madrid. In 1937, on the occasion of the celebrations of the four hundredth anniversary of the University of Lausanne he delivered an official lecture on "The Biological Aspects of Medicine." From 1940 to 1942 he was the dean of the medical faculty and introduced a revised plan of study which was of definite help to the medical student. In 1944, the senate of the University unanimously elected him rector for the years 1944 to 1946. It was during his rectorate and on his initiative that the University of Lausanne "adopted" the University of Normandy at Caen, France, completely destroyed during the war. As a token of gratitude, in 1945,this University, rising from ashes, conferred on Professor Rosselet the degree of "Doctor Honoris Causa." In 1948, on the occasion of the laying of the first stone of the new University of Normandy, he was decorated together with his friend the writer Charles Morgan, with the insignia of "Chevalier de la Legion d'Honneur."

Dr. Rosselet has published over eighty scientific papers, mostly pertaining to results of original research on heliotherapy, cellular radiosensitivity, radio-immunization, functional radiotherapy, artificial sources of light, roentgen ray and radium therapy of cancer. He was the first, in 1911, to point out the therapeutic effect and value of the infra-red rays. Also, in 1934, he was the first to combine hormone therapy with radiotherapy for the treatment of seminoma of the testicle. Among his numerous publications concerning diagnostic roentgenology, those relating to the roentgenological anatomy of the lungs are of particular significance. He has been co-editor of Scandinavian, Dutch and Swiss reviews and journals pertaining to radiology.

Above all these accomplishments, Professor Rosselet was a genuine gentleman. A man of heart, with his unassuming and spontaneously cordial attitude, he had won the respect, confidence and love of his colleagues and students. It was a particular privilege and a real pleasure for me to be his assistant from 1941 to 1944. I join the host of his grateful students and colleagues to pay tribute to his imposing scientific work and to express to Mrs. Rosselet and his sons (both of whom are medical doctors) our heartfelt sympathy.

J. N. Sarian, M.D.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, Pa. Annual meeting: Shoreham Hotel, Washington, D.C., Sept. 25–28, 1951.

American Radium Society
Secretary, Dr. J. E. Wirth, U. S. Marine Hospital, Baltimore, Md. Annual meeting: 1951, to be announced.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 713 E. Genesee St., Syracuse 2, N. Y., Annual meeting: Palmer House, Chicago, Ill., Dec. 10–15, 1950.

American College of Radiology
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6.

Section on Radiology, American Medical Association
Secretary, Dr. P. C. Hodges, 950 E. 59th St., Chicago, Ill.

Alabama Radiological Society
Secretary, Dr. W. W. Anderson, Tuscaloosa, Ala. Meets time and place Alabama State Medical Association.

Arizona Association of Pathologists and Radiologists
Secretary, Dr. R. Lee Foster, 507 Professional Bldg., Phoenix, Ariz. Two regular meetings a year. The annual meeting at time and place of State Medical Association and interim meeting six months later.

Arkansas Radiological Society
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

Atlanta Radiological Society
Secretary, D. W. W. Bryan, 490 Peachtree St., N.E., Atlanta, Ga. Meets monthly, except during three summer months, on second Friday evening.

Brooklyn Roentgen Ray Society
Secretary, Dr. J. J. Daversa, 345 75th St., Brooklyn, N. Y. Meets monthly fourth Tuesday, Oct. through April.

Buffalo Radiological Society
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

Central New York Robntgen Ray Society
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

Central Ohio Radiological Society
Secretary, Dr. F. A. Riebel, 15 West Goodale St., Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Columbus Athletic Club, Columbus, Ohio.

Chicago Roentgen Society
Secretary, Dr. B. D. Braun, 6 N. Michigan Ave., Chicago 2, Ill. Meets second Thursday of each month, October to April inclusive at the University Club.

Cincinnati Radiological Society
Secretary, Dr. E. C. Elsey, 927 Carew Tower, Cincinnati 2, Ohio. Meets last Monday of each month, September to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. J. R. Hannan, 10515 Carnegie Ave., Cleveland 6, Ohio. Meetings at 6:45 P.M. on fourth Monday of each month from October to April.

Colorado Radiological Society
Secretary, Dr. Paul E. RePass, 306 Republic Bldg., Denver 2, Colo. Meets third Friday of each month at University of Colorado Medical Center or at Denver Athletic Club.

Connecticut Valley Radiologic Society
Secretary, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday Oct. and April.

Dallas-Fort Worth Roentgen Study Club
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. J. C. Cook, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

East Bay Roentgen Society
Secretary, Dr. Dan Tucker, 434-30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

Florida Radiological Society
Secretary, Dr. T. H. Lipscomb, 30 W. Beaver St., Jacksonville, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

Georgia Radiological Society
Secretary, Dr. R. C. Pendergrass, Americus, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

Greater Miami Radiological Society
Secretary, Dr. David Kirsh, 712 duPont Bldg., Miami 32, Florida. Meets last Wednesday of each month at 8:00 P.M. at Veterans Administration Regional Office.

Houston X-ray Club
Secretary, Dr. Curtis H. Burge, 3020 San Jacinto St. Houston 4, Texas. Meets fourth Monday each month.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Illinois Radiological Society
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

Iowa X-Ray Club
Secretary, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society.

Kansas Radiological Society
Secretary, Dr. Anthony F. Rossitto, Wichita Hospital, Wichita, Kan. Meets annually with State Medical Society.

Kentucky Radiological Society
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

Kings County Radiological Society
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Los Angeles Radiological Society
Secretary, Dr. Wybren Hiemstra, 1414 S. Hope St., Los Angeles 15, Calif. Meets second Wednesday each month at Los Angeles County Medical Assn. Building.

Louisiana Radiological Society
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

* Secretaries of societies are requested to send timely information promptly to the Editor.

Louisville Radiological Society
Secretary, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Seelbach Hotel, Louisville.

Maine Radiological Society
Secretary, Dr. C. F. Miller, Central Maine General Hospital, Lewiston, Maine.

Miami Valley Radiological Society
Secretary, Dr. G. A. Nicoll, 134 Apple St., Dayton, Ohio. Meets second Friday of fall and winter months.

Michigan Association of Roentgenologists
Secretary, Dr. R. D. McDuff, 220 Genesee Bank Bldg., Flint 3, Mich.

Mid-Hudson Radiological Society
Secretary, Dr. J. W. Walton, Horton Memorial Hospital, Middletown, N. Y. Meets 8:30 P.M., fourth Tuesday each month, Sept. to May.

Milwaukee Roentgen Ray Society
Secretary, Dr. T. J. Pfeffer, 839 N. Marshall St., Milwaukee 2, Wis. Meets monthly on second Monday at University Club.

Minnesota Radiological Society
Secretary, Dr. L. A. Nash, 572 Lowry Medical Arts Bldg., St. Paul 2, Minn. Meets three times annually, once at time of State Med. Assn., and in spring and fall.

Nebraska Radiological Society
Secretary, Dr. J. E. Downing, 816 Medical Arts Bldg., Omaha, Nebr. Meets fourth Thursday of each month at 6 P.M. at Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. L. L. Robbins, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Harvard Club.

New Hampshire Roentgen Ray Society
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

New York Roentgen Society
Secretary, Dr. J. L. Olpp, 49 Ivy Lane, Tenafly, N. J. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

North Carolina Radiological Society
Secretary, Dr. J. E. Hemphill, 1420 E. Fifth St., Charlotte 4, N. C. Meets in May and October.

North Dakota Radiological Society
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings by announcement.

Northern California Radiological Club
Secretary, Dr. C. W. Wauters, 701 High St., Auburn, Calif. Meets at dinner last Monday, every second month, except June, July and August.

Ohio State Radiological Society
Secretary, Dr. E. C. Elsey, 927 Carew Tower, Cincinnati 2, Ohio.

Oklahoma State Radiological Society
Secretary, Dr. W. E. Brown, 21st & Xanthus, Tulsa 4, Okla. Three regular meetings annually.

Oregon Radiological Society
Secretary, Dr. C. T. Jessell, 214 Medical-Dental Bldg., Portland 5, Oregon. Meets monthly 2nd Wednesday, 8:00 P.M.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

Pacific Northwest Radiological Society
Secretary, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. J. M. Converse, 416 Pine St., Williamsport.

Philadelphia Roentgen Ray Society
Secretary, Dr. G. P. Keefer, American Oncologic Hospital, Philadelphia 4, Pa. Meets first Thursday each month October to May, at 8:00 P.M., in Thomson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary Dr. E. J. Euphrat, 3500 Fifth Ave., Pittsburgh 13, Pa. Meets 6:30 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

Queens Roentgen Ray Society
Secretary, Dr. J. E. Goldstein, 88-29 163rd St., Jamaica 3, N. Y. Meets fourth Monday of each month except during the summer.

Radiological Section, Baltimore Medical Society
Secretary, Dr. Harry A. Miller, 2452 Eutaw Place, Baltimore. Meets third Tuesday each month, Sept. to May.

Radiological Section, Connecticut Medical Society
Secretary, Dr. Fred Zaff, 135 Whitney Ave., New Haven, Conn. Meets bimonthly on second Wednesday.

Radiological Section, District of Columbia Medical Society
Secretary, Dr. K. C. Corley, 1835 Eye St., N. W., Washington, D. C. Meets Medical Society Auditorium, third Thursday, Jan., March, May, Oct. at 8:00 P.M.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Radiological Society of New Jersey
Secretary, Dr. Peter Gianquinto, 685 High St., Newark, N. J. Meets annually at Atlantic City at time of State Medical Society and mid-winter at Elizabeth, N. J.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. A. V. Winchell, 40 Meigs St., Rochester, N. Y. Meets monthly on last Monday from September through May, 8 P.M. at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr.

St. Louis Society of Radiologists
Secretary, Dr. H. R. Senturia, Pasteur Medical Building, St. Louis, Mo. Meets fourth Wednesday each month, except June, July, August, and September.

San Diego Roentgen Society
Secretary, Dr. R. F. Niehaus, 1831 Fourth Ave., San Diego, Calif. Meets monthly, first Wednesday at dinner.

Section on Radiology, California Medical Association
Secretary, Dr. D. R. MacColl, 2007 Wilshire Blvd., Los Angeles 5, Calif.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. Harold L. Shinall, St. Joseph's Hospital, Bloomington, Ill.

Shreveport Radiological Club
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

South Carolina X-Ray Society
Secretary, Dr. S. H. Fisher, 107 E. North St., Greenville, S. C. One meeting with South Carolina Medical Association in May, others arranged by President.

Tennessee Radiological Society
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas. Meets Galveston, Jan 19 and 20, 1951.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May inclusive. Room 203, Service Memorial Institute, 426 N. Charter St., Madison.

Utah State Radiological Society
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake

City 1, Utah. Meets third Wednesday in September, November, January, March and May.

VIRGINIA RADIOLOGICAL SOCIETY
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

WASHINGTON STATE RADIOLOGICAL SOCIETY
Secretary, Dr. R. C. Kiltz, 705 Medical-Dental Bldg., Everett, Wash. Meets fourth Monday each month, October through May, College Club, Seattle.

WISCONSIN RADIOLOGICAL SOCIETY
Secretary, Dr. Irving I. Cowan, 425 E. Wisconsin Ave., Milwaukee 2, Wis. Special meetings held during year; annual meeting each spring at Madison, Wis.

X-RAY STUDY CLUB OF SAN FRANCISCO
Secretary, Dr. M. A. Sisson, 450 Sutter St., San Francisco, 8, Calif. Meets Jan. to July, Lane Hall, Stanford Univ. Hospital; July to Dec. San Francisco Hospital.

CUBA, MEXICO AND CENTRAL AMERICA

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

SOCIEDAD MEXICANA DE RADIOLOGIA Y FISIOTERAPIA
General Secretary, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

SOCIEDAD RADIOLÓGICA PANAMEÑA
Secretary, Dr. L. Arrieta Sanchez, Apartado No. 86 Panama, R. de P. Meets monthly in a department of radiology of a local hospital, chosen at preceding meeting.

BRITISH EMPIRE

BRITISH INSTITUTE OF RADIOLOGY INCORPORATED WITH THE RÖNTGEN SOCIETY
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 P.M.
Medical Members' meeting, on third Friday in each month at 5:00 P.M., 32 Welbeck St., London, W 1.

FACULTY OF RADIOLOGISTS
Honorary Secretary, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

SECTION OF RADIOLOGY OF THE ROYAL SOCIETY OF MEDICINE (CONFINED TO MEDICAL MEMBERS)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

CANADIAN ASSOCIATION OF RADIOLOGISTS
Honorary Secretary-Treasurer, Dr. Jean Bouchard, Suite 305, 1555 Summerhill Avenue, Montreal 26, Que. Meetings January and June.

SECTION OF RADIOLOGY, CANADIAN MEDICAL ASSOCIATION
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

SOCIÉTÉ CANADIENNE-FRANÇAISE D'ELECTROLOGIE ET DE RADIOLOGIE MÉDICALES
Secretary, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

AUSTRALIAN AND NEW ZEALAND ASSOCIATION OF RADIOLOGISTS
Honorary Secretary, Dr. Alan R. Colwell, 135 Macquarie St., Sydney, N.S.W.
Honorary Secretaries, State Branches:
New South Wales, Dr. E. W. Frecker, 135 Macquarie St., Sydney.
Victoria, Dr. T. I. Tyrer, 3 Lockerbie Court, East St. Kilda.
Queensland, Dr. J. Adam, 131 Wickham Terrace, Brisbane.
South Australia, Dr. R. de G. Burnard, 170 North Terrace, Adelaide.
Western Australia, Dr. A. M. Nelson, 179-B St. Georges Terrace, Perth.
New Zealand, Dr. E. G. Lynch, 12 Bolton St., Wellington.

SOUTH AMERICA

ASOCIACION ARGENTINA DE RADIOLOGIA
Secretary, Dr. Lidio G. Mocsa, Avda. Gral Paz 151, Córdoba, Argentina. Meetings held monthly.

SOCIEDAD ARGENTINA DE RADIOLOGIA
Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

SOCIEDAD ARGENTINA DE RADIOLOGÍA, FILIAL DEL LITORAL
President, Dr. Francisco P. Cifarelli. Meets monthly second Wednesday, 7:00 P.M., 663 Italia St., Rosario.

SOCIEDADE BRASILEIRA DE RADIOLOGIA MEDICA
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

SOCIEDADE BRASILEIRA DE RADIOTERAPIA
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

SOCIEDAD COLOMBIANA DE RADIOLOGIA
Secretary, Dr. Alberto Torres Focke, Av. 34, No. 17–34, Bogota, Colombia. Meets last Wednesday of each month.

SOCIEDAD PERUANA DE RADIOLOGIA
Secretary, Dr. Julio Bedoya Paredes, Apartado, 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

SOCIEDAD DE RADIOLOGICA, CANCEROLOGIA Y FISICA MEDICA DEL URUGUAY
Secretary, Dr. Arias Bellini, Av. Agraciada 1464, Piso 13, Montevideo, Uruguay.

CONTINENTAL EUROPE

SOCIÉTÉ BELGE DE RADIOLOGIE
General Secretary, Dr. S. Masy, 111 Avenue des Allies, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

CESKOSLOVENSKÁ SPOLEČNOST PRO RÖNTGENOLOGII A RADIOLOGII V PRAZE
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland.

GDANSK SECTION, POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10.30, X-Ray Dept., Akademia Gdansk.

WARSAW SECTION, POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Meets monthly.

SOCIETATEA ROMANA DE RADIOLOGIE SI ELECTROLOGIE
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

ALL-RUSSIAN ROENTGEN RAY ASSOCIATION, LENINGRAD. USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

SCANDINAVIAN ROENTGEN SOCIETIES
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

SOCIEDAD ESPANOLA DE RADIOLOGIA Y ELECTROLOGIA
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

SCHWEIZERISCHE RÖNTGEN-GESELLSCHAFT (SOCIÉTÉ SUISSE DE RADIOLOGIE)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

SOCIETA ITALIANA DI RADIOLOGIA MEDICA
Secretary Prof. Mario Ponzio, Ospedale Mauriziano. Torino, Italy. Meets biannually.

SCIENTIFIC EXHIBIT

The Scientific Exhibit at the Fifty-first Annual meeting of the American Roentgen Ray Society (Fiftieth Anniversary Meeting) held at the Hotel Jefferson, St. Louis, Missouri, September 26–29, 1950, also showed the progress which had been made since the founding of the Society fifty years ago. The exhibit was arranged by the Scientific Exhibit Committee under the chairmanship of Dr. R. A. Arens. Many new methods for more accurate diagnosis were shown and color was used in numerous illustrations of microsections, gross specimens and lesions, which greatly enhanced the effect of the exhibits. Television was also demonstrated to have found an important place by permitting consultation on films between the large hospitals and the small community hospitals situated at some distance from one another. The value of radioactive isotopes in diagnosis and therapy was demonstrated. Another feature of the exhibit was the new and greatly improved view boxes which were used for the first time. These demonstrated the exhibits to much greater advantage than the boxes formerly used. A great deal of interest was displayed in the scientific exhibits and the exhibitors gave generously of their time in explaining the essential features in detail. The Scientific Exhibit was disposed in various sections on the meeting room floor and thus permitted study of the exhibits at every opportunity without loss of time.

The following is a brief description of each scientific exhibit together with the awards given.

Roentgenographic Features of Slipped Capital Femoral Epiphysis. Armin Klein, M. D., Robert J. Joplin, M.D., John A. Reidy, M.D., and Joseph Hanelin, M.D., Massachusetts General Hospital, Boston, Massachusetts. The roentgenographic features of slipped capital femoral epiphysis were shown in the earliest and later stages of slipping. These features were seen in the anteroposterior and lateral projections of both hips, taken by a standard technique. Slipping may be evident in only one of these views. Slipping of the contralateral hip may be recognized early if standard type roentgenograms are taken at frequent intervals. The earliest manifestations of slipping become obvious when roentgenograms are compared with "normals" of corresponding osseous maturation. Anteroposterior and lateral roentgenograms of "normal" hips, of boys and girls aged one to seventeen, were presented as a basis for comparison. This exhibit was awarded a Certificate of Merit.

Letterer-Siwe's Disease—Problems in Diagnosis and Treatment. Eugene L. Saenger, M.D., and Ralph J. Johansmann, M.D., University of Cincinnati, Cincinnati, Ohio. Letterer-Siwe's disease is the infantile form of reticuloendotheliosis with a characteristic clinical picture of fever, skin rash, anemia and roentgenological changes in lung and bone. The exhibit showed the skin lesions, roentgen and pathological findings.

Translumbar Arteriography: Our Experience in over 400 Cases. Parke G. Smith, M.D., Arthur T. Evans, M.D., Benjamin Felson, M.D., and Edward C. Elsey, M.D., Cincinnati General Hospital and Christ Hospital, Cincinnati, Ohio. The exhibit consisted of a roentgenologic and photographic demonstration of the utilization of arteriography in certain conditions. A demonstration, by photography, of the technique of translumbar arteriography and the necessary equipment was presented. In addition, there were view boxes with a number of arteriograms from interesting cases as well as a plastic demonstration of aortic puncture. This exhibit was awarded a Silver Medal.

Radiating Spicules—a Nonspecific Manifestation of Bone Disease. Otto H. Grunow, M. D., and Lauren V. Ackerman, M.D., Washington University School of Medicine, St. Louis, Missouri. Original roentgenograms, photographs, drawings, and descriptive material were shown demonstrating the large number of conditions, such as osteogenic sarcoma, metastatic malignancy, syphilis, and osteomyelitis in which spicule formation or sunburst reactive periosteal patterns may be found.

Accessory Equipment for Lateral Roentgenography of the Hip Joint. E. F. Merrill, M.D., H. B. Crawford, M.D., and C. F. Bridgman, B.A. (by invitation), Rochester General Hospital, Rochester, New York. The exhibit demonstrated by means of kodachrome transparencies the use of equipment which improves the quality and simplifies the making of

lateral roentgenograms of the hip joint. Although primarily designed for use in the operating room during orthopedic operations, it is also very helpful in the roentgenographic department. The equipment consists of a new type of hip joint localizer, a cassette holder, and a tunnel. Roentgenograms made with the aid of this equipment were shown.

Cephalopelvimetry. Fred O. Coe, M.D., Radiological Clinic, Drs. Groover, Christie and Merritt, Washington, D. C. A method of cephalopelvimetry was presented which is unique in that the size of both the pelvis and fetal skull can be determined by routine examination whether the presentation is cephalic or breech. Abnormalities of the fetus were shown; position of placenta and all details of pelvic measurements.

Accessory Sacroiliac Articulations, with Arthritic Changes. Lee A. Hadley, M.D., Syracuse, New York. Accessory articulations may occur between the ilium and the sacrum in addition to the normal sacroiliac joints. The most common is an articular facet which projects downward and medially from the posterior sacral iliac spine to a point on the sacrum just lateral to the second posterior sacral foramen. Arthritic changes noted were narrowing and irregularity of joint space, exostoses of the joint margins and sclerosis of the underlying bony tissue. Some of the joints become ankylosed. Most of these patients complain of low back pain and some of them indicate the vicarious joint as tender to deep pressure. A review of the roentgenographic studies of 200 consecutive private patients having these symptoms revealed 33.5 per cent showing evidence of accessory sacroiliac articulations. Arthritic changes were seen in 36.7 per cent of these joints. The exhibit consisted of dissected specimens and roentgenograms illustrating this condition.

Abdominal Arteriography. David Shapiro, M.D., Everett L. Pirkey, M.D., Gerald M. Peterson, M.D., and Joseph C. Bell, M.D., University of Louisville School of Medicine, Louisville, Kentucky. The exhibit consisted of thirty 14 by 17 inch roentgenograms as follows: four normal abdominal arteriograms; five cases of Leriche's syndrome; one renal cyst—two illustrations, one of retrograde urogram and one of abdominal arteriogram; three carcinomas of the kidney—retrograde urogram and abdominal arteriogram in each; two cases of horseshoe kidney—abdominal arteriogram in each; one hypoplastic kidney—retrograde urogram and abdominal arteriogram; two abdominal aneurysms—abdominal arteriogram in each; one aneurysm of left iliac artery shown by abdominal arteriography; aneurysm of right renal artery—retrograde urogram and abdominal arteriogram; one saddle thrombus demonstrated by abdominal arteriography; congenital absence of a kidney—intravenous urogram and abdominal arteriogram of one case. Also included in the exhibit was a discussion of the technique, indications for abdominal arteriography, the value of abdominal arteriography in differential diagnosis in abdominal lesions, and so forth. This exhibit was also awarded a Silver Medal.

Paraduodenal Hernia. P. B. Parsons, M.D., Norfolk General Hospital, Norfolk, Virginia. The exhibit dealt with herniation about the ligament of Treitz and demonstrated the genesis of several encapsulation patterns. In the exhibitor's experience these lesions are fairly common.

Diaphragmatic Hernias in Infancy. W. A. Evans, M.D., and J. O. Reed, M.D., Children's Hospital of Michigan, Detroit, Michigan. Diaphragmatic hernias in infancy were reviewed with special attention to various types, differential diagnosis from other conditions, and ultimate prognosis. Because of the urgency of the diagnosis in the newborn, this aspect was stressed since the earliest possible operative repair is consistent with the best results.

The Diaphragm. J. A. Campbell, M.D., J. G. Lorman, M.D., J. W. Wilson, M.D., and M. M. Manalan, M.D., Indiana University Department of Radiology, Indianapolis, Indiana. This exhibit was prepared as a teaching instrument for Indiana University post-graduate and undergraduate students in radiology. An attempt was made to establish the range of normal variation and the roentgenographic appearance of the diaphragm in various age groups. A classification of the abnormalities of the diaphragm was presented and illustrative cases of each pathological group given. This did not represent a demonstration of all possible abnormalities, but included many of the more common entities which emphasize the variety of conditions encountered and frequently identified by simple roentgenographic methods. The roentgenographic recognition of these lesions is familiar to all experienced roentgenologists, but it was thought that a review of this subject according to a more orderly classification would be of some general interest.

Roentgen Diagnosis of Diseases of the Spinal Cord and Nerve Roots. Ernest H. Wood, M.D., and Emil H. Schnap, M.D., Neurological Institute of New York, New York, New York. The exhibit consisted of reproductions of plain roentgenograms of the spine and myelograms. Photographs were used to illustrate myelographic technique and artists' sketches of pathological specimens were included. The first part of the exhibit illustrated abnormalities demonstrable in plain roentgenograms of the spine, chiefly spinal cord tumors. A number of frames illustrated the technique of myelography, together with numerous technical errors which are to be avoided. The major portion of the exhibit consisted of myelograms illustrating methods of diagnosis of spinal cord tumors, herniated intervertebral discs, and the more common vertebral lesions which involve the spinal cord.

Antigenic Pneumonitis: Its Relationship to the Collagen Diseases. L. R. Sante, M.D., and J. P. Wyatt, M.D., St. Louis University School of Medicine, St. Louis, Missouri. Diseases usually listed as affecting collagen tissues vary widely in nature. A number of these are apparently associated with allergic manifestations. Azotemic edema is consistently observed in some of these diseases, indicating a special pattern of onset and involvement. This exhibit was illustrated with a large number of color photographs of specimens, both gross and microscopic. This exhibit was awarded the Bronze Medal.

Aortic Arch Anomalies. D. R. Harrington, M.D., and H. M. Stauffer, M.D., Temple University Hospital, Philadelphia, Pennsylvania. Anomalies of the aortic arch are not rare. Many are clinically significant, roentgenologically demonstrable, and amenable to surgery. Examples of the more common ones were shown together with their embryology and clinical history.

Dural Sinus Venography: A New Roentgen Technique. Charles T. Dotter, M.D., Bronson S. Ray, M.D., and Howard S. Dunbar, M.D., The New York Hospital, New York, New York. The exhibit comprised examples of contrast visualization studies of the intracranial dural venous sinuses, illustrating the normal and certain pathological conditions encountered. This exhibit was awarded a Certificate of Merit.

The Roentgen Diagnosis of Genitourinary Tuberculosis. John K. Lattimer, M.D., Veterans Administration and Columbia University, New York, New York. Eighteen full color paintings were presented to show the pathology behind as many pyelograms and roentgenograms of scrotums, prostates, ureters (mounted side by side) from the Genitourinary Tuberculosis Research Center conducted by the Veterans Administration and Columbia University.

Developments in Cardiovascular and Cerebral Angiography. Wendell G. Scott, M.D., Wayne A. Simril, M.D., and William B. Seaman, M.D., Washington University School of Medicine, St. Louis, Missouri. This exhibit consisted of photographs, diagrams and representative cardiovascular and cerebral angiograms illustrating some of the more typical pathological disorders and pointing out some of the diagnostic pitfalls inherent in these procedures. The techniques of injection were described.

Roentgenologic Television: A Service for the Small Community Hospital. J. Gershon-Cohen, M.D., M. B. Hermel, M.D., S. M. Berger, M.D., Victor Kremens, M.D., and D. M. Sklaroff, M.D., Jewish Hospital, Philadelphia, Pennsylvania. This consisted of a demonstration of television apparatus now used for roentgenologic consultation between the staff at Jewish Hospital in Philadelphia and private offices six and a half miles distant. The range and limits of apparatus and technique were exhibited.

Thorium X Treatment of Skin Cancer, Keratoses, Radiation Sequelae. J. J. Shers, M.D., and William E. Howes, M.D., Brooklyn Cancer Institute, Brooklyn, New York. The exhibit consisted of about forty-five color transparencies in 5 by 7 inch mounts with clinical data in each mount. The transparencies showed the before and after cases treated by thorium X successfully with no evidence of radiation sequelae.

Expanding Type of Uterine Radium Applicator: Treatment of Carcinoma of the Cervix. Edwin C. Ernst, M.D., Barnard Free Skin and Cancer Hospital, DePaul Hospital, St. Louis, Missouri. The most recent type of expanding radium applicator for the treatment of carcinoma of the cervix uteri was illustrated. Kodachrome photographs showed the various radiation effects before and after the application of various doses of radium and including subsequent follow-ups of both the favorable and unfavorable cases. Special dosage charts and typical clinical records of various stages of carcinoma of the cervix were illustrated.

Diagnostic Use of Radioactive Isotopes. L. Reynolds, M.D., K. E. Corrigan, Ph.D., and H. S. Hayden, Ph.D., Harper Hospital, Detroit, Michigan. This exhibit illustrated types of cases which were discussed in a paper on the same subject given in the scientific session. The differential diagnosis of various shadows in the roentgenogram and clinical lesions which show no roentgen shadow were demonstrated by means of radioactive tracers.

Unusual Radiosensitivity of a Malignant Teratoma of the Mediastinum and a Mesothelioma of the Pleura. Samuel Richman, M.D., Veterans Administration Hospital, Richmond, Virginia. The great advances in thoracic surgery have forced the role of radiation therapy, in respect to the treatment of intrathoracic neoplasms, further into the background. The only exceptions are those cases of lymphosarcoma and Hodgkin's disease of the lymph nodes. All publications emphasize the point that radiation therapy will fail to reduce the size of mediastinal tumors unless they are of lymphatic origin. The purpose of this presentation was to demonstrate the effectiveness of roentgen therapy, although of short duration so far, in a malignant teratoma of the mediastinum and a mesothelioma of the pleura. Both of these neoplasms have been considered in the past to be extremely resistant to radiation therapy.

Cobalt 60 for Cancer Therapy. Joseph L. Morton, M.D., William G. Meyers, M.D., George W. Callendine, M.S., and Alan C. Barnes, M.D., Ohio State University Medical Center, Columbus, Ohio. This exhibit was designed to illustrate methods of treatment with interstitial, intracavitary and surface plaque applicators using cobalt 60 as a gamma-ray emitter. A practical method of handling, dosage calculation, and actual measurement was described in sufficient detail to permit development of similar handling elsewhere. A number of the handling techniques vary from that employed with radium. Special equipment design was illustrated. Research and clinical investigations with low atomic weight applicator sheaths indicate that many new applicator shapes are feasible. Roentgenograms of actual cases were employed to illustrate the advantages of this type of therapy. Method of securing radioactive cobalt, and preliminary measurements were outlined. Dosage calculations, including adaptation of Paterson and Parker charts, and the exhibitors' own isodose curves with small scintillation counter were illustrated. The exhibit encompassed three years of research and development of radioactive cobalt therapy at this institution.

The Dose-Time Relationship for the Cure of Squamous Cell Carcinoma: Its Derivation and Significance. J. Robert Andrews, M.D., and Thomas O. Coppedge, M.D. (by invitation), Bowman Gray School of Medicine, Winston-Salem, North Carolina. This exhibit showed the dose-time relationship for the radiotherapeutic cure of squamous cell carcinoma. The derivation of this relationship by the graphical analysis of published data was explained and it was shown how, by such analyses, the curative dose for squamous cell carcinoma can be defined in respect to over-all treatment time.

Plastic Surgical Repair of Radiation Injuries Including Those of Atomic Origin: Prevention of Chronic Radiation Lesions and Possible Extension of Radiation Therapy. James Barrett Brown, M.D., Frank McDowell, M. D., and Minot P. Fryer, M.D., Washington University School of Medicine, Department of Surgery, St. Louis, Missouri. Radiation burns are seen in large numbers; the lesions are progressive and dangerous as the ultimate stage is carcinoma. The number of burns does not seem to be decreasing and the source of the exposure, and often fantastic histories of the course of the lesion would seem to make the situation one of major importance to radiologists, surgeons and all branches of medicine as well as to the patients. Since the lesion is progressive, the most effective treatment in serious lesions is wide deep excision and repair with free skin grafts or flaps. A paradox is that this plastic surgical treatment is best done early or in a quiescent stage rather than in an ulcerated or infected stage, to obtain the best results. Extension of radiation therapy might be possible if the practice is carried out of excising and replacing skin that has been heavily irradiated, *before* it becomes hopelessly damaged. Means of supplying additional blood supply to irradiated areas may be had by proper permanent blood carrying pedicle flaps, and it is with this idea of cooperation that this exhibit was presented. Atomic radiation lesions were presented with illustrations of repair, and in the next war surgery will be called on in this additional field to substitute construction for destruction. Mounted photographs and photomicrographs in color of lesions with their repairs were pre-

sented in plexiglass frames, with descriptions of plates supplied for individual study. These records represented details of repair of a very large series of patients from all parts of the country.

Dose Distribution in Cervix Cancer Treated by Parametrial Needles and Intracervical Tandem. Russell L. Nichols, M.D., and J. W. J. Carpender, M.D., University of Chicago, Chicago, Illinois. This exhibit presented dose distribution as calculated in eight cases of cancer of the cervix uteri treated by parametrial needles and intracervical tandem. The dose was calculated by locating the needles as placed in the pelvis by an orthographic pelvimetry method and subsequently summating the contribution of individual needles to the various points in the pelvis. This exhibit was awarded a Certificate of Merit.

Kerosene Intoxication: A Clinical and Experimental Study. H. D. Kerman, M.D., E. S. Reed, M.D., S. Leiken, M.D., R. L. Taylor, M.D., and E. L. Pirkey, M.D., University of Louisville School of Medicine, Louisville, Kentucky. A roentgenographic and clinical study of the pulmonary changes produced by the accidental ingestion of kerosene in small children was presented. Follow-up studies were also included. The experimental results in laboratory animals were also presented in an attempt to determine the pathogenesis of these pulmonary changes.

Photographs of Past Presidents of the American Roentgen Ray Society and Others. U. V. Portmann, M.D., Cleveland Clinic Foundation, Cleveland, Ohio. This exhibit consisted of photographs of the Past Presidents of the American Roentgen Ray Society; photographs of the Presidents of the International Congress of Radiology, and a photograph of the 1901 meeting of the American Roentgen Ray Society. This exhibit was awarded a Certificate of Merit.

COMMERCIAL EXHIBIT

One of the most valuable and interesting features of any annual meeting of the American Roentgen Ray Society is the Commercial Exhibit and that at the Fifty-first Annual Meeting of the Society (Fiftieth Anniversary Meeting) held at the Hotel Jefferson, St. Louis, Missouri, September 26–29, 1950, was no exception. The background of the booths was blue and the signs showing the names of the exhibitors were done in blue and gold to carry out the anniversary color scheme. The exhibit was an unusually extensive one; thirty-seven exhibitors had reserved a total of seventy-three booths, and much that was new in engineering design was shown. Many of the exhibitors featured the Fiftieth Anniversary of the Society with appropriate displays which added greatly to the interest of the exhibits. Here, too, was emphasized to no small degree the great progress which had been made in fifty years as demonstrated by the greatly improved apparatus for diagnosis and therapy and the advanced engineering designs. The exhibits were placed in rooms and sections adjacent to the registration, the meeting room and the scientific exhibit and this disposition gave those in attendance ample opportunity to visit each of the booths. Time was also allotted in the program for a study of the exhibits. The Society as always extends its thanks and appreciation to all of the exhibiting firms for their great share in the success of the meeting.

The following firms were represented in the Commercial Exhibit:

Amperex Electronic Corporation, Brooklyn, New York; *Ansco*, Binghamton, New York; *Automatic Seriograph Corporation*, College Park, Maryland; *Buck X-Ograph Company*, St. Louis, Missouri; *Calculex Company*, Dallas, Texas; *Coreco Research Corporation*, New York, New York; *E. I. du Pont de Nemours & Company*, Wilmington, Delaware; *Eastman Kodak Company*, Rochester, New York; *Eldorado Mining and Refining, Ltd.*, Ottawa, Ontario; *Eureka X-Ray Tube Corporation*, Chicago, Illinois; *Fairchild Camera and Instrument Corporation*, Jamaica, New York; *H. G. Fischer & Company*, Franklin Park, Illinois; *Franklin X-Ray Corporation*, Philadelphia, Pennsylvania; *General Electric X-Ray Corporation*, Milwaukee, Wisconsin; *High Voltage Engineering Corporation*, Cambridge, Massachusetts; *Paul B.*

Hoeber, Inc., New York, New York; *Kelley-Koett Manufacturing Company*, Covington, Kentucky; *Liebel-Flarsheim Company*, Cincinnati, Ohio; *Macalaster Bicknell Company*, Cambridge, Massachusetts; *Machlett Laboratories*, Springdale, Connecticut; *Mallinckrodt Chemical Works*, St. Louis, Missouri; *F. Mattern Manufacturing Company*, Chicago, Illinois; *Micro X-Ray Recorder*, Chicago, Illinois; *Thomas Nelson & Sons*, New York, New York; *North American Philips Company*, Mt. Vernon, New York; *Pako Corporation*, Minneapolis, Minnesota; *Picker X-Ray Corporation*, New York, New York; *W. B. Saunders Company*, Philadelphia, Pennsylvania; *Schering Corporation*, Bloomfield, New Jersey; *Frank Scholz X-Ray Engineering Service*, Boston, Massachusetts; *Standard X-Ray Company*, Chicago, Illinois; *Charles C Thomas, Publisher*, Springfield, Illinois; *Victoreen Instrument Company*, Cleveland, Ohio; *Webster Photocraft*, Webster Groves, Missouri; *Westinghouse Electric Corporation*, Pittsburgh, Pennsylvania; *Winthrop-Stearns*, New York, New York; *Year Book Publishers*, Chicago, Illinois.

NEW OFFICERS

AMERICAN ROENTGEN RAY SOCIETY

At the Fifty-first Annual Meeting of the American Roentgen Ray Society held at the Hotel Jefferson, St. Louis, Missouri, September 26–29, 1950, the following officers were elected for the year 1950–1951: *President-Elect:* Dr. H. Dabney Kerr, Iowa City, Iowa; *1st. Vice-President:* Dr. Harold G. Reineke, Cincinnati, Ohio; *2nd Vice-President:* Dr. Ralph M. Caulk, Washington, D. C.; *Secretary:* Dr. Barton R. Young, Philadelphia, Pennsylvania (re-elected); *Treasurer:* Dr. Wendell G. Scott, St. Louis, Missouri (re-elected); *Member of the Executive Council:* Dr. Clyde A. Stevenson, Temple, Texas. The *President* is Dr. B. P. Widmann, Philadelphia, Pennsylvania, and the *Chairman of the Executive Council* is Dr. Paul A. Bishop, Philadelphia, Pennsylvania.

ANNOUNCEMENT OF NEW PUBLICATION

A valuable aid to nuclear physicists and engineers, radiochemists, biophysicists, and other workers in the rapidly expanding field of nuclear physics is now available in the tables of *Nuclear Data* recently compiled by the National Bureau of Standards. These tables, which may be obtained from the Government Printing Office, are to be followed by supplements of new material at six-month intervals.

The initial volume of the tables, together with the supplements, will present a comprehensive collection of experimental values of half-lives, radiation energies, relative isotopic abundances, nuclear moments, and cross sections. Decay schemes and level diagrams, over 125 of which are included in the tables now ready, are to be provided wherever possible.

At present over 1,000 new measurements of different nuclear properties are being reported each year in some 30 different journals and in the reports of many different laboratories. The reactor engineer and the industrial or medical user of radioactive tracer materials, as well as the nuclear physicist, are thus in need of a listing of available data which can automatically be kept up-to-date.

The National Bureau of Standards, with the assistance of the Oak Ridge National Laboratory, the Brookhaven National Laboratory, the Massachusetts Institute of Technology, and the University of California Radiation Laboratory, is making the first effort to present a continuing compilation in this rapidly developing field. The present tables and the supplements to follow are therefore designed for easy assimilation of new material in loose-leaf form.

All the more recent values of a given nuclear property are listed in the tables. Thus, from the degree of uniformity of the results, the reader can tell at a glance which nuclear constants now appear fairly certain and which are still quite doubtful. The references to over 2,000 original papers

make it possible for the research worker to evaluate the details of previous investigations and to design experiments to resolve existing discrepancies.

Circular 499, *Nuclear Data*, 310 pages, is available from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C. The price of $4.25 a copy includes the cost of three supplements (about 60 pages each) which the purchaser will automatically receive at six month intervals. Remittances from foreign countries must be made in United States exchange and must include an additional sum of one-third the publication price to cover mailing costs.

BRITISH AMERICAN EXCHANGE FELLOWSHIPS IN CANCER RESEARCH

British American Exchange Fellowships in Cancer Reseach of the American Cancer Society, awarded by the Society upon recommendation of the Committee on Growth of the National Research Council, are offered to citizens of the United States for advanced training and experience in Great Britain in specialized fields of investigation pertaining to the problem of cancer. Similar fellowships are awarded by the British Empire Cancer Campaign to British scientists for study in the United States. The Society and the Committee on Growth welcome the cooperation of universities and hospitals in making known these opportunities to suitable candidates.

These fellowships are awarded by the American Cancer Society to provide specialized training for American investigators in Great Britain where opportunities exist for study in facets of research in malignant disease not widely available in this country. Training for an equal number of young British scientists selected by the Campaign will be provided in this country. The Society, the Committee on Growth, and the British Empire Cancer Campaign believe that the training of young men and women in the many complex disciplines of modern scientific thought and techniques are fundamental to a sound approach to the problem of human cancer.

Candidates will be favored who express intention of following a career in a discipline applicable to the study of growth. In evaluating fellowship applications the Committee will keep in mind potential applicability of the proposed training program to problems of neoplastic growth in specialized scientific areas in which superior facilities exist in Great Britain.

Fellowships are open to citizens of the United States who possess the degree of Doctor of Medicine, Doctor of Philosophy, or Doctor of Science. They are intended for young men and women embarking upon a career in clinical medicine or basic research, and also for more mature candidates desiring to extend their fields of competence in these fields. Applicants must be able to demonstrate that they have qualifications necessary to pursue investigation in the fundamental sciences or in clinical medicine.

Applications should state the institution where the fellow plans to work in Great Britain; the individual under whom the fellow desires to work; what problem he intends to investigate; when he wishes to start.

Fellowships will be awarded for a period of one year.

The annual stipend will be £1,000 ($4,020.00). An allowance of $600.00 is made for travel to the site of the fellowship in Great Britain.

University staff appointment, with teaching duties agreeable to the fellow, is permitted, provided it carries no additional salary and provided it is acceptable to the Committee on Growth, the American Cancer Society, and the British Empire Cancer Campaign. No other remunerative work will be permitted during the tenure of the fellowship.

Fellowship appointments are subject to the condition that once accepted, they will not be vacated or the place of work changed within the period of tenure without the

consent of the Committee on Growth, the American Cancer Society, and the British Empire Cancer Campaign.

Application forms for British American Exchange Fellowships in Cancer Research may be procured from and submitted at any time to the Executive Secretary of the Committee on Growth, Division of Medical Sciences, National Research Council, 2101 Constitution Ave., Washington 25, D. C. Favorable action by the Committee on Growth takes the form of a recommendation to the American Cancer Society, and is subject to approval by the Society. Fellowships will be made effective at the convenience of the institution and the fellow.

MAURICE LAMM BLATT MEMORIAL FUND LECTURE

The Pediatric Staff of the Cook County Hospital announces that the second Maurice Lamm Blatt Memorial Fund Lecture was given by Dr. John Caffey, Clinical Professor of Pediatrics at Columbia University, on October 9, 1950, in the medical amphitheater of Cook County Hospital. Dr. Caffey's subject was "Infantile Cortical Hyperostosis and Vitamin A Poisoning."

DETROIT ROENTGEN RAY AND RADIUM SOCIETY

At a recent meeting of the Detroit Roentgen Ray and Radium Society the following officers were elected for the ensuing year: *President*, Dr. William A. Evans, Detroit, Michigan; *Vice-President*, Dr. Horace Porter, Jackson, Michigan; *Secretary-Treasurer*, Dr. James C. Cook, Detroit, Michigan

FLORIDA RADIOLOGICAL SOCIETY

The following officers of the Florida Radiological Society have been elected to serve for 1950–1951: *President*, Dr. F. K. Hurt; *Vice-President*, Dr. John J. McGuire; *Secretary-Treasurer*, Dr. Thos. H. Lipscomb.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

MYELOGRAPHY WITH WATER-SOLUBLE CONTRAST, WITH SPECIAL REGARD TO THE NORMAL ROENTGENPICTURE. *Acta radiologica*, Supplementum LXXV. By Sigfrid Arnell, Chief, Roentgenological Department, Lasarettet, Gävle. Paper. Pp. 85, with 61 illustrations. Esselte Aktiebolag, Stockholm, Sweden, 1949.

In this very thoughtfully and carefully prepared monograph the writer summarizes the results of more than twenty years' study of the lower spinal canal and its contents, together with his experiences in contrast myelography.

The monograph is divided into 3 chapters, some with subsections which are as follows:

Chapter I. The embryonic development of the caudal part of the vertebral canal.

Chapter II. Anatomical conditions. Nine sub-sections as follows:

1. The spinal cord
2. Pia mater
3. Arachnoidea and the subarachnoidal space
4. The subdural space
5. The nerve-roots
6. Arachnoiditis cystica et proliferans
7. Dura mater spinalis
8. The epidural tissue
9. The spinal canal

Chapter III. The contrast myelography with the following sub-sections.

1. History.
2. Account of experiments with abrodil-myelography on living subjects.
3. General points concerning the contrast-filling of the subarachnoidal space.
4. A short account of the technique now used for myelography with abrodil.

The embryonic development of the lower spinal canal is briefly considered. Anatomical conditions are dealt with in detail, particularly the epidural tissues, the dura and arachnoid, together with their relationship to the bony confines of the spinal canal, the spinal cord and nerve roots. Many anatomical developmental variations in the subarachnoid space are described and illustrated, especially in its caudal extremity.

The history of the development of contrast myelography is brief but pertinent, the bibliography is comprehensive and includes most publications dealing with the subject of myelography. A detailed discussion of the author's own work and technique, both experimental and in living subjects, is included.

This monograph is an important contribution in the field of myelography and should be of interest and value to all students of this subject, to neurosurgeons, neurologists and orthopedic surgeons and possibly other physicians as well.

JOSEPH C. BELL, M.D.

CONGENITAL ANOMALIES OF THE HEART AND GREAT VESSELS. Clinicopathologic Study of 132 Cases. By Thomas J. Dry, Robert L. Parker, H. Milton Rogers, Jesse E. Edwards, Howard B. Burchell, and Arthur H. Bulbulian of the Mayo Clinic. Cloth. Price, $4.50. Pp. 68, with 80 illustrations. Springfield, Illinois: Charles C Thomas, 1949.

This beautifully produced book presents photographs of specimens and of models made from them in twenty examples of congenital heart disease. These were the more representative and most completely studied of 132 cases in which clinicopathological data were available. The monograph is based on an exhibit and the latter type of presentation is adhered to. Each case therefore is accompanied by a brief text on the nature of the anomaly, brief histories of the patients illustrated, the principal clinical features of the anomaly given tersely and a statement of the incidence of the anomaly in the series. There are reproductions also of the posteroanterior roentgenogram and usually the electrocardiogram.

Presentations of this character always add significantly to the literature much as do the case histories. In a field where autopsy verification is not often available in patients who have been studied clinically with any thoroughness, the present monograph is obviously important. Yet one completes his perusal of the volume with a vague sense of frustration. No attempt is made to establish a pattern by which one might be assisted in the diagnosis of the next congenital cardiac that appears. For this reason, the monograph could hardly be called a text. It is

rather a compendium of cases which the specialized worker might wish he had seen himself but, as a second choice, is grateful for such well illustrated material.

The findings on cardiac catheterization are included when available but apparently this was not often the case and this phase of the work-up is not given any prominence. Unavoidably, a novice would gain the impression that they are incidental data rather than the crux to the understanding of the pathological physiology. The fact is that the contributors to this monograph are well known workers in the physiological field. It is too bad that their material dictated a rather static presentation.

Marcy L. Sussman, M.D.

The Causation and Treatment of Delayed Union in Fractures of the Long Bone. By Kenneth W. Starr, O.B.E., E.D., M.B., B.S., M.S., F.R.C.S., Surgeon, Sydney Hospital, New South Wales; Visiting Surgeon, Concord Military Hospital; Consulting Plastic Surgeon, Faculty of Dentistry, University, of Sydney; Member of the Court of Examiners, Royal Australasian College of Surgeons; Lt.-Col. (R. of O.), A.A.M.C., late Officer Commanding Surgical Division. Cloth. Price, $9.00. Pp. 215, with 106 illustrations. Butterworth & Co., Ltd., 4–6 Bell Yard, Temple Bar, London, England; The C. V. Mosby Company, 3207 Washington Boulevard, St. Louis 3, Missouri, 1947.

The volume, which is a Jacksonian Prize Essay, is published with the permission of the Council of the Royal College of Surgeons of England. It is divided into three sections. The first discusses the morphogenesis of bone as to structure, chemistry, reconstruction and the relation between structure and function. The second deals with the healing of fractures, the anatomical structures involved in their repair and the factors which may influence the part taken by these structures. The third covers in detail the etiology and treatment of delayed union from the historical, therapeutic and clinical aspects. Included is a discussion of the management of problems encountered in the treatment of fractures. Fifty briefly described cases are reported in an appendix.

This essay, which is interspersed with quotations of historical interest, is a compendium of six hundred and fifteen references with the author's comments and reflections. The bibliography is quite inclusive and as such is a good review of the literature to the date of the volume's publication This reviewer, in many instances, had difficulty in distinguishing which material was being quoted and which was the author's. This remark, adverse as it may appear, cannot be denied. In his introduction Starr frankly admits "to borrowing without shame from the scientific riches stored in the bibliography." The latter would have been made more inclusive by additional borrowing from the writings of Axhausen and Phemister. There is no reference to the work of Hertz on vitamin C.

The volume is profusely illustrated. The publishers are to be criticized for miniature reproductions of several tables.

The author's pleasantly written and logically organized work is recommended to those interested in this phase of surgery. They will be stimulated by his review but will not agree with many conclusions and concepts which are didactically presented.

Frank P. Walsh, M.D.

Carcinoma of the Larynx. *British Journal of Radiology*, Supplement No. 3. By F. Baclesse, M.D., "Chef de Service" of the X-ray Department, Foundation Curie, Paris. With a Statistical Report on Cases Treated with X Rays Only. By R. W. Gunderson, B.Sc., D.M.R.T., F.R.C.S. (Eng.), The Meyerstein Institute of Radiotherapy, The Middlesex Hospital, London. Paper. Price, 25s. Pp. 68, with numerous tables and illustrations. British Institute of Radiology, 32, Welbeck Street, London, England, 1949.

The first portion of this monograph is devoted to a careful classification of the types of carcinoma encountered in the larynx based on the sites of origin. The different varieties are illustrated by diagrams, drawings of the laryngoscopic images and soft tissue roentgenograms of the neck, and the prognostic significance of these findings is emphasized.

The statistical portion of the paper includes 341 cases treated from 1919 to 1940. The results obtained in 42 patients treated with teleradium were so poor that this method was discontinued. In a group of 215 cases treated with roentgen rays alone the five year survival rate for those without nodes was 33 per cent and for those with nodes 1.3 per cent. The best results were obtained in those patients in whom severe reac-

tions were avoided by the protraction of treatment over relatively long periods of time. Tumor doses varying from 5,000 to 9,600 roentgens were given in periods varying from forty to seventy days in this group. Much of the work was carried out with small portals (usually three in number) varying from 3 by 4 cm. to 5 by 6 cm. in size.

Charles L. Martin, M.D.

Brookhaven Conference Report. Biological Applications of Nuclear Physics. July 12–27. 1948. Paper. Price, $1.50. Pp. 154, with 67 illustrations and 32 tables. Brookhaven National Laboratory, Associated Universities, Inc., Upton, New York, 1948.

This volume is a collection of rather brief papers presented at the Conference held at Brookhaven National Laboratory during the period of July 12–27, 1948. The conciseness of the presentations, however, should not be a deterrent to readers interested in the impact of Nuclear Physics on the Biological Sciences, because the reports are excellent and varied. Many authors bring fresh points of view on the subject, which are stimulating and entertaining.

The effects of radiation on aqueous solutions and on enzyme systems are discussed by A. O. Allen, D. Mazia, and E. S. G. Barron; those on genetic systems are presented by K. C. Atwood, E. Caspari, B. P. Kaufman W. R. Singleton, and D. Bonner. The various effects of radiation in mammalians are described by G. W. Gowen, F. P. Ellinger, A. Edelman and C. L. Prosser.

This group of papers is followed by others concerned with the applications of radioisotopes to the study of biologically important processes or to the analysis of compounds of biological importance. Thus D. Pressman reports on the zone of activity of antibodies, L. B. Flexner *et al.* deal with capillary permeability, F. C. Steward with salt metabolism of plants and W. T. Bowen with the mineral metabolism of insects.

Harzards are covered by W. P. Norris, B. S. Wolf, and F. P. Cowan; whereas, biochemical techniques and applications are treated by M. Gibbs, L. M. Sharpe, J. Sacks, N. S. Radin and A. S. Keston.

It is impossible to review cirtically such a collection of papers beyond stating that it should be widely ready by both scientists and practicing radiologists because of its timeliness and broad coverage.

L. D. Marinelli

ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor: T. Leucutia, M.D., Harper Hospital, Detroit 1, Michigan

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ROENTGEN DIAGNOSIS

SKELETAL SYSTEM

Key, J. Albert. Intervertebral-disc lesions in children and adolescents. *J. Bone & Joint Surg.*, Jan., 1950, *32A*, 97–102.

In spite of the fact that low back pain, with or without sciatica, is a frequent complaint and cause of disability in adults, this condition is rarely encountered in children and adolescents. When pain in the low back is encountered in a child or adolescent, one expects to find roentgenographic evidence of disease, especially tuberculosis, neoplasm or epiphysitis. The clinical picture differs from that usually seen in adult life. If one admits, Key believes, that the patients with relatively mild symptoms are suffering from intervertebral disc lesions, then the condition is common in early life, but is rarely diagnosed. The typical disc syndrome may also occur in early life but is rare. The prognosis is good, and nearly all of the patients recover as a result of conservative treatment.

The three positive physical findings most frequently encountered are: (1) pain on deep pressure over the fifth lumbar disc, between the spines of the fifth lumbar and the first sacral vertebra; (2) limitation of straight leg-raising on one or both sides; (3) pain and limitation of movement in the low back. The patient may be referred because of pain, a limp, ease of fatigue, difficulty in sleeping, or trouble in stooping. The disc lesions seem to occur more frequently in boys than in girls, and may or may not follow a specific injury. In more severe cases with sciatic radiation, pain may be elicited by pressure over the gluteal, sciatic, popliteal or posterior tibial nerves, and the ankle joint on the affected side may be diminished or absent.

The roentgenograms of the spine, lumbar area, reveal nothing abnormal unless congenital anomalies are present and these are not believed to be factors in the production of low back or sciatic pain. However, roentgenograms should be taken in order to rule out destructive disease (tuberculosis or neoplasms) or spondylolisthesis.

The treatment recommended is the use of a firm level bed, postural exercises, support, manipulation and in about 10 per cent of cases, operation is justified if symptoms do not yield to conservative treatment.—*R. S. Bromer, M.D.*

Kaplan, Abraham. Herniated intervertebral discs producing contralateral symptoms and

signs. *Bull. Hosp. Joint Dis.*, Oct., 1949, *10*, 207–215.

Routine use of pantopaque myelography in persistent and recurrent back pain has been strongly advocated. This routine will eliminate guess work, permit accuracy in the diagnosis of herniation of intervertebral discs, prevent unnecessary exploration, and enhance smooth recovery.

Recently Murphy reported 2 cases, with operative confirmation, presenting contralateral signs and symptoms of lumbar intervertebral disc protrusion.

The author's report of 2 cases confirms Murphy's observation and is the second such report to appear.

Finding a defect in the oil column during myelography on the contralateral side prompted a wider surgical approach. A herniated disc was found as indicated by the filling defect on the myelogram and not on the side of clinical signs and symptoms, as would have been anticipated. Guided by the latter, only a unilateral surgical approach would have been made with negative operative findings and no relief of symptoms to the patient.

In the 2 cases reported, there was no bulging on the side of the signs and symptoms, but considerable bulging produced by disc herniation was seen on the opposite side. The nerve root, overlying the herniated disc was stretched. There was complete relief of symptoms and a clinical cure was obtained after operative removal of the disc.

The above cases bring out a further indication of the urgent need for thorough routine myelographic studies of patients with recurrent and persistent back pain.—*W. H. Shehadi, M.D.*

Thelander, H. E. Epiphyseal destruction by frostbite. *J. Pediat.*, Jan., 1950, *36*, 105–106.

The author reports the case of a nine-year old boy who complained of pain and swelling of the digital joints of the right hand. He had suffered a sufficiently severe frostbite two and a half years previously that amputation of the right hand was considered. Physical examination revealed that the fingers of the right hand were shorter than those of the left hand. The examination was otherwise normal except that the right hand became blue and painful on chilling.

A roentgenogram showed absence of the epiphyses at the proximal and distal interphalangeal joints of the right hand, partial loss of the joint spaces and irregularity and increased bone density of the diaphyses. The affected phalanges were shorter than the corresponding phalanges of the opposite hand.

The author is surprised at the absence of literature on this condition. He feels that the mechanism producing the changes is prolonged ischemia with possibly thrombosis of small vessels.—*R. M. Harvey, M.D.*

Sherman, Mary S. Osteomalacia. *J. Bone & Joint Surg.*, Jan., 1950, *32A*, 193–206.

The author in this paper gives an interesting account of the controversy which raged concerning the question whether or not rickets and osteomalacia were entirely separate diseases. The historical introduction is complete and covers the literature in excellent fashion. Albright and his associates have pointed out that the term osteomalacia should be reserved to describe any disorder of adults which results in the presence in the bones of abnormal amounts of osteoid tissue. Any condition which causes the body's calcium stores to be depleted sufficiently can cause osteomalcia. Such depletion can come about either through insufficient absorption of calcium or through excessive loss.

The author's discussion of the possible etiologies of osteomalacia is modified from Albright's classification: (A) Insufficient vitamin D, of which there may be simple lack or such as occurs in gastrointestinal disorders where difficulty in absorption of calcium from the intestinal tract occurs. (B) Renal acidosis in which are included tubular insufficiency without glomerular insufficiency and the Fanconi syndrome. (C) Idiopathic hypercalcuria. In this condition a low kidney threshold for calcium apparently develops in some patients. They excrete continuously a large amount of calcium in the urine, no matter how depleted their skeleton may become. Albright and his associates included in their classification a fourth group which comprised the transient osteomalacia which may be seen immediately following removal of a parathyroid adenoma.

There are available sixty-five papers, reputedly reporting some 99 cases of osteomalacia from the United States and Canada. If one excepts the cases reported by Albright and his associates, there are among all the other papers, reports of 2 proved cases, only 1 of which

had pathological examination. Six other cases had suggestive histories and findings, but the evidence was insufficient for proof. On the other hand, the fact that Albright has been able to collect 6 unquestionable cases and 3 others in which the conditions for the development of osteomalacia were certainly present leads one to suppose that the disorder is not so much rare as it is undiagnosed. Such was the case with 1 of the 2 cases reported by Sherman in this paper.

The 2 patients described in this paper are the fourth and fifth pathologically proved cases of osteomalacia to be reported from North America. Sherman believes that it is obvious that osteomalacia is not so rare in North America as it has been believed to be. It is also obvious that it is by no means limited to females. Furthermore, since in this country simple dietary deficiency is a rare cause, osteomalacia most often appears as a complication of some other disorder. Therefore, if the possibility of bone changes be kept in mind, more biopsies will be done and the diagnosis will probably be made with increasing frequency. Osteomalacia (adult rickets) is a condition in which the bone matrix (osteoid tissue) is formed normally, but fails to calcify. The term osteomalacia should be reserved to describe this condition and no other.—*R. S. Bromer, M.D.*

Rothschild, Carl E. Aseptic necrosis of the femoral head simulating tuberculosis. *Bull. Hosp. Joint Dis.*, Oct., 1949, *10*, 226–232.

In aseptic bone necrosis, there is interruption of the blood supply to the bone but with no concomitant or resultant infection of the involved bone. This most commonly involves the femoral head where weight bearing is a serious complicating problem.

Among causes of interruption of the blood supply to the femoral head are mentioned, fracture of the femoral neck, dislocation of the hip, slipped epiphysis, congenital hip dislocation after reduction, Perthes' disease, caisson disease, radium or roentgen therapy of malignant disease and, rarely, no known cause or accident, as in the case reported.

Roentgenologically, aseptic necrosis appears as an area of uniform relative density followed later by collapse of bone, loss of cartilage and irregularity of the articulations. In the healing stage, clear cystic areas are seen within the dense bone representing bone absorption prior to the calcification.

The condition is easily differentiated from tuberculosis of bone, especially of the hip joint, which is characterized by the following factors: (1) bone atrophy appears early and is present throughout the course of the disease; (2) bone destruction, if not early, invariably occurs later, starting outside weightbearing areas and is characteristically irregular; (3) often small sequestra are detached from apposing articular surfaces; (4) there is absence of new bone formation, except in secondary infection; (5) bone destruction of the innominate bone causes progressive enlargement of the acetabulum with apparent upward and inward displacement ("wandering acetabulum").

A unique case of aseptic necrosis presenting all the recognized criteria for the diagnosis of tuberculosis is reported. The pathological material obtained at operation, however, proved the diagnosis of aseptic necrosis.—*W. H. Shehadi, M.D.*

Harris, W. Robert. The endocrine basis for slipping of the upper femoral epiphysis; an experimental study. *J. Bone & Joint Surg.*, Feb., 1950, *32B*, 5–11.

For this study, an apparatus was designed to determine the shearing strength of the upper tibial epiphysis in the rat. Observations were made with this instrument on normal animals, on animals receiving growth-hormone, and on animals receiving estrogen. Estrogen was selected for the experiments because it is well known that it produces typical histological changes even when given in relatively small amounts. Harris found that when the epiphysis separates from the diaphysis, the plane of cleavage is constant, passing through the third layer of the epiphyseal plate. The first layer consists of resting cartilage cells on the epiphyseal plate. The first layer consists of resting cartilage cells on the epiphyseal side of the plate. The second layer is made up of proliferating cartilage cells arranged in orderly rows parallel to the long axis of the bone. The third layer is formed as new cartilage is added to the advancing edge of the plate by the division of cartilage in the second layer. The cartilage cells which were already present, enlarge as they grow older, forming a layer of hypertrophied cartilage cells. The fourth layer is formed by the precipitation of mineral salts in the intercellular substance and this is usually termed as the "zone of provisional calcification."

It is through the third layer that the plane of cleavage occurs.

Harris found that growth-hormone decreases and sex-hormone increases the shearing strength of the epiphyseal plate. These changes are due to alterations produced by these two hormones in the thickness of the third layer of the plate. He suggests that these findings may be of significance in providing an anatomical basis for slipping of the upper femoral epiphysis in man, especially when it is associated with the adiposogenital syndrome or with rapid adolescent growth.—*R. S. Bromer, M.D.*

Hughes, E. S. R. Acute deposition of calcium near the elbow. *J. Bone & Joint Surg.*, Feb., 1950, *32B*, 30–34.

In this paper, 3 cases of localized deposition of calcium salts deep to the origin of the common extensors of the forearm with acute symptoms clinically indistinguishable from "tennis elbow" are described. Nine similar cases were found, reported in the literature. The characteristic symptoms are acute onset of pain, tenderness and swelling in the region of the lateral epicondyle. Roentgenograms show a dense shadow below the epicondyle. In patients treated by early operation it was evident that this shadow was due to the deposit of a viscous fluid, consisting largely of calcium phosphate in the origin of the common extensor aponeurosis. With conservative treatment the fluid may absorb rapidly and the acute symptoms may subside but the more chronic features of "tennis elbow" tend to persist.

Hughes suggests that "tennis elbow" is caused by a lesion probably an adventitious bursitis in the tissue space between the tendon of origin of the forearm extensors and the capsule of the radiohumeral joint, and that it is the sudden precipitation of calcium phosphate at the site which causes the lesion he describes. The acute calcification near the elbow joint is compared with similar calcification which may occur in the insertion of the supraspinatus tendon. He advises operative treatment.— *R. S. Bromer, M.D.*

Milch, Henry. Roentgenographic differentiation between torsion and rotation in fractures of the forearm. *Bull. Hosp. Joint Dis.*, Oct., 1949, *10*, 216–225.

Axial deviations of a torsional nature, until recently have been considered to be of minor importance. Torsional deformity after fracture (accidental or surgical osteotomy) of bones of forearm is gaining wider recognition as a significant cause of limitation of motion. Furthermore, medicolegal considerations present an added problem.

Therefore, the recognition and prevention of torsional malalignment are of major significance in treatment of any type of break of axial continuity of either bone of the forearm.

Two tests are utilized: (1) determination of the presence of cross-sectional incongruence which is applicable in recent fractures; (2) demonstration of abnormal configuration of the projection of the whole bone. This is applicable at any stage of torsional deformities, irrespective of cause.

Cross-sectional incongruence arises from the fact that the long bones are not ideally circular, but have on cross section, a larger and a smaller diameter.

Accurate reduction should ensure accurate apposition of the largest diameter of both bones in addition to avoiding inaccurate alignment, angulation, transposition, and overriding. A discrepancy will occur when the large diameter of one fragment is in apposition with a short diameter of the other and/or the long axes are not exactly on the same plane.

In rotation, regardless of the position of the bone in relation to the film, the upper and lower ends of the bone will maintain normal anatomical relationships. While in torsion, there will be a change within the anatomical relationship of the bone. Thus, it is important that the entire bone be included on the film.

While the extremity is in a plaster cast, the problem is more difficult, especially when distortion occurs. It is suggested that a steel wire be incorporated in the cast. The shadow on the roentgenogram can be used for comparison on subsequent examinations. The absence of rotation will be characterized by identical projection of the shadow of the steel wire on the roentgenograms.—*W. H. Shehadi, M.D.*

Murray, R. C., and Forrai, Elemér. Transitory eosinophilia localised in the knee joint after pneumarthrography. *J. Bone & Joint Surg.*, Feb., 1950, *32B*, 74–83.

The purpose of this paper as stated by the authors is not to discuss the clinical value of pneumarthrography of the knee joint but to record that the introduction of gas into a joint, as one might gather from the literature, is not a process without reaction. There is, in fact,

a specific reaction. It was observed clinically that effusion often appeared in the joint after air arthrography, or that pre-existing effusion increased in size. These effusions were studied in a group of 60 consecutive cases in which air injection was followed by exploration of the knee joint. In about 100 cases oyxgen was used instead of air for the purpose of arthrography. Solely on the basis of clinical observation the authors believe that the synovial reaction is less frequent after the injection of oxygen than after the injection of air, and the effusions that do occur are usually smaller.

The following conclusions were reached after the study of 200 cases: (1) the introduction of air or oxygen into the knee joint is followed by a specific reaction characterized by transient localized eosinophilia in synovial membrane and fluid; (2) complications after meniscectomy seem to be more frequent when operations are performed during the phase of eosinophil reaction; (3) the significance of these observations lies in the fact that as far as the authors know, localized tissular eosinophilia has not been produced experimentally in humans. They suggest that through experimental production of eosinophilia in the knee joint by injecting gas, an important and easily accessible technique is available by which to pursue research on the causes of eosinophilia.—*R. S. Bromer, M.D.*

Winkler, Harry, and Young, Cabell, Jr. Fractures of the tibial plateau. *South. M. J.*, Jan. 19, 1950, *43*, 35–39.

The authors review the anatomy of the knee joint giving the relationship and functions of the ligaments, and stress the point that the great strength of this joint is due to the strong ligamented attachments.

The recent trend has been to do open reductions on depressed fractures of the tibial condyles. This trend has resulted in a large group of papers which emphasize the bad prognosis in such injuries and the frequent necessity for operative correction of the condylar masses. The authors state that the impression left by these papers was contrary to the experiences in their clinic.

Between 1938 and 1948, 903 fractures of the tibia were treated by the authors. Of this group, 117 fractures of one or both condyles were involved. In this survey the authors tried to correlate the relationship between the types of lesion and the prognosis and the effect of treatment on prognosis. In brief, it was found that in a large series of cases representing all degrees of injury to the condylar mass, operative interference was seldom indicated and that conservative care plus time did not give the bad results often reported. Furthermore, it was found that remarkably good function could be recovered in the knee joint in spite of roentgenographic evidence of moderate compression of part of the articular surface.

The treatment advocated by the authors consists of plaster or brace immobilization until roentgenograms show evidence of satisfactory union. In most instances, six weeks were sufficient. Prolonged immobilization detracts from the freedom of the joint and is unnecessary as a preventive of deformity. Operative replacement is seldom necessary except in cases of extreme displacement. Compound fractures or fractures in an obvious pre-existing joint disease were not included in the studies.

In general, the poor results of this type of treatment was directly proportional to the depth of depression of the condylar mass. Accompanying fractures of the fibula had little or nothing to do with the ultimate outcome. Many of the cases showed collateral ligament, cartilage, or cruciate damage in the early weeks following the removal of the plaster. This almost invariably disappeared or decreased to a minimum between six and twelve months after the fracture. In some instances simple physiotherapy such as heat, massage and quadriceps drill was necessary. No true statement could be made as to when arthritic changes might be expected to occur. They developed in some cases within weeks after the removal of the plaster, and in others after several years of relative freedom.

There is one statistical analysis and four illustrative drawings.—*J. G. Snead, M.D.*

McMurray, T. P. Footballer's ankle. *J. Bone & Joint Surg.*, Feb., 1950, *32B*, 68–69.

The injury which the author regards as peculiar to the professional footballer, especially those over the age of twenty-five years, is the result of repeated minor strains of the anterior ligament of the ankle joint. It is characterized by pain and tenderness localized to the area of strain. Roentgenologic examination shows a bony outgrowth into the capsule of the joint from the anterior margin of the tibia or from the upper surface of the neck of the astragalus.

The liability to ligamentous strain arises from the position of plantar flexion in which the foot is held at the moment of contact with the ball, especially when the ball is "dead." A football may be kicked with any part of the foot but in order to control its direction the foot must be held in full equinus to ensure the largest possible area of contact between the foot and the ball. In this position the extensor muscles which normally protect the dorsal capsule of the ankle joint are at a mechanical disadvantage and the strain of the blow is borne largely by the ligament. In Association football this position is used constantly in kicking the ball; in Rugby football it is used only in drop-kicking. In punting and place-kicking the joint is in less equinus and is protected by the extensor muscles.

The roentgenographic appearance varies according to the duration of the symptoms. In the early stages there may be nothing more than a slight periosteal roughening on the anterior aspect of the lower end of the tibia. Later, a bony ridge may be seen extending forward from the surface of the tibia at the level of the attachment of the anterior capsule of the joint. Occasionally a similar outgrowth is seen projecting upwards and slightly backwards from the neck of the astragalus. Owing to the position and extent of the bony rim the roentgenographic appearances are suggestive of osteoarthritis of the ankle joint with lipping of the articular margin of the tibia, but there is in fact no involvement of the articular surfaces and the outgrowth lies slightly above the articular margin which is clear and unaffected.

Operative removal of the abnormal bone mass appears to be the only certain method of cure. —*R. S. Bromer, M.D.*

Lauge-Hansen, Neils. Ligamentous ankle fractures; diagnosis and treatment. *Acta chir. Scandinav.*, 1949, *97*, 544–550.

Ligamentous ruptures about the ankle joint may give rise to as much pain and disability as actual malleolar fractures in this area. The diagnosis of such ligamentous detachments, however, is often overlooked on routine roentgenograms of the ankle.

The author lists three types of ligamentous fractures about the ankle joint, which may be diagnosed by special roentgen studies:

(1) Supination-abduction fracture: Rupture or detachment of the calcaneofibular ligament and posterior talofibular ligament occurs at the attachment of these ligaments at the tip of the lateral malleolus, or on the calcaneous and talus. Roentgen examination in the frontal plane, with adduction of the hind portion of the foot, and fixation of its distal portion, will reveal a distinct varus position of the talus in the tibiofibular mortise.

(2) Pronation-abduction fracture: Detachment of the deltoid (medial) ligament may be diagnosed by noting a valgus position of the talus in special frontal projections obtained with abduction of the hind portion of the foot.

(3) Pronation-eversion fracture: In addition to rupture of the deltoid ligament there is detachment of the lateral malleolar fragment, and interosseous tibiofibular ligament. Roentgenograms in the frontal plane with the foot in eversion will demonstrate valgus position of the talus and increase in width of the tibiofibular syndesmotic space.

Employing the special techniques mentioned above, the author found 31 ligamentous ankle fractures among 106 lesions in the year 1948. —*E. C. Lasser, M.D.*

Kleinberg, Samuel, Horwitz, Thomas, and Sobel, Robert. Pes cavus. *Bull. Hosp. Joint Dis.*, Oct., 1949, *10*, 252–268.

This article reviews the subject of cavus of the foot. It is described as a relatively common deformity, involving both the soft tissues and the bones, which is characterized by an "abnormally high arch, contracted plantar tissues, shortening of the foot, inversion of the foot and contracted toes."

An etiological classification is given which divides the cases into a small congenital group present at birth and a much larger acquired group. The latter is further divided into those cases which follow an attack of anterior poliomyelitis, those associated with several progressive lesions of the nervous system such as Friedrich's ataxia and peroneal muscular dystrophy, and those associated with inflammatory, vascular and traumatic lesions. A final large idiopathic group completes the classification.

The roentgenographic findings vary from practically no abnormality seen in the early stages to marked deformities seen later. The moderately advanced case will show a shortening of the foot associated with a very high longitudinal arch. The metatarsal arch is de-

pressed, the toes are clawed, the heel is inverted and there is atrophy of the foot and leg.

Surgical reconstruction corrects the deformity reasonably well in the severe and chronic cases and prevents further progression of the lesion.—*F. H. Squire, M.D.*

Chandler, Fremont A., and Kaell, Harry I. Osteoid-osteoma. *Arch. Surg.*, Feb., 1950, *60*, 294–304.

The authors report 7 cases of osteoid-osteoma and cover the entity from the standpoint of etiology, symptomatology, pathology, and treatment.

Etiology is unknown; it occurs more often in males than females and usually during the second or third decade of life. At least 40 per cent occur in the femurs, 60 per cent in other bones.

Symptomatically, the most prominent sign is pain which varies from mild and intermittent to severe and persistent in type. Localized tenderness is a frequent finding but rarely is there any temperature elevation. Roentgenographically the appearance early is usually a small (1 cm.) area of radiolucence; later the area is surrounded by considerable sclerosis. Pathologically, the tumor is benign in character and arises from the proliferation of the osteogenic mesenchyme. Early osteoblasts are seen in the stroma. Finally the intercellular substance calcifies forming patches of osteoid. Later the osteoid calcifies. The cause of the perifocal sclerosis is unknown. Laboratory tests are of no help. The treatment of this entity is complete surgical excision and no cases of recurrence have been reported where the excision has been complete.—*L. S. House, M.D.*

Jones, Frederick Wood. Classical gout. *Brit. M. J.*, March 11, 1950, *1*, 561–567.

The author (himself a victim of gout) writes in a readable, witty, informative and informal manner of classical gout. He accepts the definition, that gout "consists in a disturbance of purine metabolism marked by excess of uric acid in the blood." In the next sentence, he is careful to add that, "all that may be said of the association of hyperuricaemia with gout is that 'hyperuricaemia almost invariably occurs at some stage in the course of the disease'."

The writer questions the premise of older physicians that gout is an articular disease or an arthritic condition of the metatarsophalangeal joint of the great toe. He quotes several authors who state that "radiological changes (in the joint) which are present in about one-third of all cases of gout occur late in the disease and are non-specific. The abundance of witty and colorful phrases which the writer chooses to describe the clinical signs of the disease (particularly pain) justifies the reading of this article in its entirety.

The writer describes the vascular and nervous supply of the foot in great detail before submitting his explanation for cause of pain and periarticular swelling in classical gout. The periarticular arterial anastomoses and the corresponding plexuses of periarticular veins are stressed. Moreover, "connecting these two complex (vascular) systems there are the 'canoux dérivatifs' described by Sucquet. It is this arrangement that permits each segment of the limb to behave as a self-regulating circulatory unit: arterial blood may be short-circuited into the venous system in the region of every joint by means of arteriovenous channels."

The writer concludes, "It is a simple (perhaps too simple) matter to picture that some vasomotor upset of this very obvious anatomical vascular arrangement normal to the big toe is responsible for the symptoms of podagra and that the similar conditions prevailing in the periarticular anastomoses of other joints account for the less frequent manifestations of so-called 'articular' gout." He adds that perhaps classical gout "might find its rightful place among such an assemblage of vasomotor syndromes as Weir Mitchell's erythromelalgia, causalgia, Raynaud's disease, acrocyanosis, and the many other conditions in which autonomic nerve involvements in the limbs are the outstanding manifestations."—*R. F. Niehaus, M.D.*

Buchtala, V., and Fuchs, K. H. Zur Ätiologie der Looserschen Umbauzonen (schleichende Callusbildung) und der Ermüdungsbrüche am Knochen. (The etiology of Looser's zones [creeping callus] and fatigue fractures.) *Chirurg*, March, 1950, *21*, 143–147.

The authors are in essential agreement with Looser's original conclusions and discard as inadequately substantiated the inflammatory and vascular theory of Deutschländer and Moritsch, respectively. Looser's zones and fatigue fractures, considered as a single entity, differ from ordinary fractures in that they result from minimal trauma and have a prolonged healing time, even under ideal condi-

tions. For similar reasons, they may be regarded as pathological fractures. According to the adherents of the mechanical stress theory, spondylolisthesis, aseptic necrosis and cortical tears properly belong in the same category.

Various intensities of vibratory stimuli were applied to dogs to effect graded, traumatic insults. Weekly roentgenograms were taken and the animals were sacrificed at similar intervals. The roentgenographic findings were divided into four stages: (1) a localized area of increased density and a minimal periosteal reaction; (2) marked periosteal reaction and partial disintegration of compact bone; (3) a well defined radiolucent area, corresponding to Looser's transformation zone, which resembled a fracture but there was no external evidence of fracture; and (4) bone regeneration. Although this was the usual sequence, some cases showed necrosis and sequestration. The histopathological picture paralleled Looser's findings and resembled callus in which osteoid tissue predominated.—*J. Zausner, M.D.*

Düben, W. Umbauzone an der kindlichen Sitz-Schambeinverbindung und ihre differentialdiagnostische Bedeutung. (Transformation zones of the juvenile ischiopubic junction; their differential diagnostic significance.) *Chirurg*, March, 1950, *21*, 148–152.

Changes of the ischiopubic junction, variously described as osteochondritis, osteochondrosis or osteochondropathy, represent another manifestation of Looser's transformation zones. Three of the author's 6 cases had a pathological condition of the contralateral side, namely congenital hip dislocation, coxa vara or Perthes' disease. Such associated lesions are not essential to the transformations since these occur in the absence of other pathology. The inferior pubic arch is the weakest part of the anterior pelvic ring; in the region of the junction with the ischium, moreover, are attached the adductor muscles with their strong antagonistic actions, the anterior flexors and the posterior extensors.

Roentgenographically two types are described: (*a*) an irregular, elliptical, translucent area with a border of reactive sclerosis; (*b*) a similar lesion without the calcified zone. Initially there is a bud-like prominence, resembling callus, on the concave side of the arch. The callus is later replaced by trabeculated bone and there may be no sign of the protuberance.

Differential diagnosis: Osteomyelitis shows a poorly circumscribed area, but the decalcification is seldom limited to the region of the ischiopubic junction. In tuberculosis, the lesion starts on the convex side and is characterized by bone atrophy, sequestration, abscess and fistulae. Luetic osteochondritis must be considered. Tumors are rare. Fractures present no difficulties.—*J. Zausner, M.D.*

Hirsch, Wolfgang. Diffuse Osteosklerose bei aleukämischer Myelose. (Diffuse osteosclerosis in aleukemic, myelogenous leukemia.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, March, 1950, *72*, 591–595.

Diffuse endosteal osteosclerosis was discovered incidentally on a chest film of a patient with aleukemic myelogenous leukemia. The osteosclerosis is differentiated from osteopetrosis (Albers-Schönberg), among other features, by (1) forty year old patient without symptoms (including spontaneous fractures) related to the skeletal system; (2) no evidence of similar disease in the patient's family; (3) the associated blood picture and the clinical picture of aleukemic leukemia; and (4) the increase of the osteosclerosis over a five year observation period.—*H. G. Moehring, M.D.*

Lichenstein, Louis. Aneurysmal bone cyst; a pathological entity commonly mistaken for giant-cell tumor and occasionally for hemangioma and osteogenic sarcoma. *Cancer*, March, 1950, *3*, 279–289.

The present article deals with a condition designated as aneurysmal bone cyst. The condition represents a fairly common pathological entity, although it seems not to be generally recognized as such, being currently mistaken for an unusual type of giant cell tumor occasionally for hemangioma and even osteogenic sarcoma. From a study of 8 cases, the author presents the clinical, roentgenographic and pathologic features of the condition.

The lesion is essentially a solitary, localized, and expanded fibrous lesion honeycombed by an enormously dilated, plexiform, vascular bed. It develops in the vertebral column, flat bones and in the long bones. In a long bone, it is likely to be the shaft that is affected, rather than the bone end. In the vertebral column, it is usually the neural arch of one or perhaps two adjacent vertebrae that is involved, although occasionally the body may be cystically transformed. In a flat bone, the lesion may be encountered at the bone end or at some distance from its articulation.

The condition is often observed in patients between the ages of ten and twenty years. The major complaints are usually pain accentuated by movement, and awareness of a palpable bony swelling that has developed insidiously. If the end of a bone adjacent to a joint is involved, there may be a limited range of painful motion. With involvement of a vertebra there may be present, in addition to sharp pain, signs of pressure on the spinal cord or its nerve roots. There may frequently be a history of trauma to the area.

The roentgenographic appearance is roughly that of an ovoid, bulging lesion with its long axis in the general direction of the bone within which it arises. It may vary from 2 or 3 cm. to 7 cm. or more in greatest dimension. The original cortex is largely, if not completely destroyed, but the lesion is delimited peripherally by a thin shell of periosteal new bone. The roentgenographic projection of the interior of the lesion appears relatively radiolucent, indistinctly mottled, and often delicately or coarsely trabeculated. The trabeculation is not due to actual osseous septa but rather to spurs and ridges on the endosteal surface of the expanded shell.

Internally, the spongy bone and marrow are completely replaced by a peculiar fibrovascular tissue. This tissue is characterized cytologically by the presence of numerous pools of blood, contained within what appear to be strikingly dilated, preformed vascular channels, and bordered by supporting connective tissue. The latter shows hemorrhage, more or less conspicuous giant cell reaction, and reparative new bone formation. Aneurysmal bone cyst is entirely benign and responds satisfactorily to simple currettement and apparently also to radiation therapy.

The possible etiology and differential characteristics of the lesion are discussed.—*F. McCrea, M.D.*

Buckles, Maurice G., and Lawless, Edward C. Giant cell tumor of ribs. *J. Thoracic Surg.*, March, 1950, *19*, 438–443.

A case of giant cell tumor of the rib is reported. At the time of removal it extended from the fifth rib to the iliac crest and from the umbilicus posteriorly almost to the spine. The large size may be due to its duration of approximately eight years. Removal at the time of biopsy (six years previously) was abandoned due to excessive hemorrhage. Two courses of roentgen therapy (2,400 r and 3,600 r) had no effect on the tumor.

Review of the literature reveals only 9 authentic cases reported. The symptomatology and clinical findings are discussed. Due to the inadequate series, it is difficult to draw any definite conclusions as to the proper treatment. The tumor is essentially benign, although local recurrence and malignancy have been reported. The duration between onset and treatment of the tumor does not influence the success of the definite treatment. While roentgen therapy may be effective in some cases, it apparently had no effect on the authors' case, either in controlling pain or diminishing the size of the tumor. Invasion of the soft parts is not uncommon and may be the explanation of the occasional recurrence. The treatment of choice is early surgical excision, while the tumor is still small, and before it invades the soft parts. —*F. M. Reis, M.D.*

Christopherson, William M., and Miller, A. J. A re-evaluation of solitary plasma-cell myeloma of bone. *Cancer*, March, 1950, *3*, 240–252.

The authors review the literature concerning solitary plasma cell myeloma. Out of 94 cases recorded, they have selected 49 which appear to be cases of true solitary plasma cell myeloma. These, they have divided into three groups and tabulated. Group I represents those followed for three or more years without dissemination. To this group they add 3 cases. Group II, those in which an autopsy was performed and a solitary lesion found. Group III, those followed one to three years. The remainder of the 94 cases were not included because the recorded data were insufficient to establish the solitary nature of the lesions, the follow-up periods were of less than one year duration, or because they subsequently proved to be multiple myeloma.

The age in the 49 selected cases ranged from nineteen months to seventy-two years with the greatest number of patients in the sixth decade. Males were affected three times as often as females. The sites of predilection were the vertebrae, femur and pelvis. The symptoms in decreasing frequency were pain, more severe when associated with trauma of the spine, swelling, palpable mass, fracture. Bence-Jones protein was present in only 9 per cent of the cases.

Two types of bone lesions were found: one with the appearance of a giant cell tumor, the

other representing a purely destructive lesion.

The authors conclude that (1) solitary plasma cell myeloma of bone appears to be a well established entity unrelated to multiple myeloma; (2) the neoplastic nature of plasma cell myeloma of bone is suggested by its unicellular composition, although the natural history of the lesion lends some doubt to this concept; (3) diagnosis depends on roentgenographic bone surveys, bone marrow examinations, clinical evaluation, and, of necessity, on a prolonged period of observation; and (4) the prognosis of true solitary myeloma of bone is always good.—*P. B. Lockhart, M.D.*

Goluboff, Nathan. Infantile cortical hyperostoses (Caffey-Smyth syndrome). *Canad. M. A. J.*, Feb., 1950, *62*, 189–191.

Infantile cortical hyperostoses is a new clinical entity first reported by Caffey in 1945. The author reports a case of this disease occurring in a four and a half months infant and reviews the findings in the previously reported 21 cases.

The etiology is unknown and none of the cases demonstrated any scorbutic or rachitic changes. The majority of the cases showed changes before the age of seven months with the oldest occurring at two and a half years of age.

The characteristic clinical findings are facial swellings, irritability, fever and bone pain. The course is benign and self-limiting and lasts from two to nine months.

Laboratory findings usually show an elevation of the white blood cell count, elevated sedimentation rate and anemia. The alkaline phosphatase is usually elevated and represents the only abnormal finding of the blood chemistry. Roengen studies demonstrate cortical hyperostoses generally involving the mandible, clavicles, ribs and extremities. In some instances a soft tissue swelling will precede changes in the underlying bones. Biopsy has shown only hyperplasia of the lamellar cortical bone.

Complete recovery occurs in all cases. No treatment of any specific value has been found.—*A. E. Imler, M.D.*

Brailsford, James F. Sclerosing conditions of bone. *Brit. J. Radiol.*, Feb., 1950, *23*, 83–91.

The most striking instance of generalized increase in density is a hereditary dysplasia, known as Albers-Schönberg's disease. It occurs in families, and can be brought out by consanguinity of parents. It occurs in varying degrees: it may be incompatible with independent life, developing and being demonstrable in utero; or it may be discovered accidentally later in life after trauma. The affected bone is expanded, soft, and increased in calcium content. The fragility has led some to consider it a form of fragilitas ossium, or osteogenesis imperfecta. The overgrowth of bone in severe cases encroaches upon the cranial foramina, producing cranial nerve palsies, and it replaces the marrow spaces, producing anemia.

An unrelated cause of generalized density is prolonged ingestion of fluorine. Other conditions which have at times been mistaken for Albers-Schönberg's disease are Paget's disease, carcinomatosis, and osteomyelosclerosis of anemia and leukemia. The similarity is superficial; the roentgen characteristics are usually easily distinguishable, and the clinical pictures are quite different.

Paget's disease begins in one bone, although it may be multicentric in origin, and progresses slowly. At first there is subperiosteal proliferation with decalcification, followed by increased deposition of calcium with coarsened texture. There are three types: the osteolithic, the osteoporotic, and the lithocystic. Malignant metaplasia occurs at times, usually subperiosteally, though it may be intramedullary.

Metastases from carcinoma of the prostate and occasionally the stomach or other viscera produce increased density of bone beginning as localized deposits but becoming generalized. The clinical picture usually resolves any doubt that may arise.

Localized increase in bone density occurs in osteochondritis, osteomyelitis, osteoid osteoma, which is probably also inflammatory, gummata, tuberculosis, melorheostosis, and sclerosing sarcoma of bone.—*E. F. Lang, M.D.*

Ude, Walter H. Osteitis condensans ilii; the possible relationship to juvenile epiphysitis. *Journal-Lancet*, Feb., 1950. *70*, 81–82.

The author reports 6 cases of osteitis condensans ilii which are briefly described. The condition was observed between the ages of twenty-six and sixty-six years, 5 of the affected persons being females and 1 a male.

Osteitis condensans ilii is usually discovered by roentgen examination. It consists of a localized sclerosis of one or both ilia along the sacroiliac joints, without any visible alterations in

the joint proper or in the adjacent borders of the sacrum. In early cases the involvement may be limited to the lower portion of the auricular process of one ilium.

The etiology is unknown. Rendich and Shapiro, on the basis of a microscopic study of a biopsy specimen obtained during the performance of a surgical fusion of the joint, described the condition as a non-inflammatory calcium condensation in the osseous tissue with obliteration of the evident former lacunae. All of their patients were examined because of low back pain which occasionally simulated the pain seen in herniated disc.

In the author's 6 cases there were concomitant changes in the spine suggestive of sequelae of vertebral epiphysitis (Scheuermann's disease). Three of the cases had an associated degenerative process in the region of the symphysis pubis. In the youngest patient with unilateral involvement there was also a narrowing of the sacroiliac joint on the affected side.

The simultaneous occurrence of osteitis condensans ilii and vertebral epiphysitis makes the author believe that the two lesions are of common etiology. The condensation of the bone represents a secondary manifestation in the weight-bearing sacroiliac joint which was primarily affected by a juvenile epiphysitis. The narrowing of the sacroiliac space observed in the unilateral involvement constitutes an additional proof in support of this theory indicating that variations in the curvatures of the spine produced by the vertebral epiphysitis influence the directional strain placed on the sacroiliac joints, thus accounting for the secondary changes. In bilateral involvement the strain is on both sides leading to an identical appearance.—*T. Leucutia, M.D.*

Fairbank, H. A. Thomas. Osteopathia striata. *J. Bone & Joint Surg.*, Feb., 1950, *32B*, 117–125.

Osteopathia straita is a very unusual affection and is characterized by striation of the skeleton and particularly of the metaphyses of the long bones. Comparatively few cases have been reported in the literature. The cause is unknown. The author considers that it is the result of a congenital developmental error. Voorhoeve suggested that the striated bones he had described in his original contribution were related to dyschondroplasia and osteopoikilosis, the three disorders being variants of the same fundamental error, with the first forming a link between the other two. Fairbank hesitates to accept such a view, particularly with respect to osteopoikilosis.

There appear to be no symptoms definitely referable to the bone dysplasia. Vague recurrent pains in the joints, with or without a little swelling, may be noted. The roentgen examination shows as a striking feature striation of varying degree. This may affect all bones except those of the skull and the clavicles. In the long bones the striation affects principally the metaphyses, dense lines running parallel to the long axis of the bones which can be traced for a considerable distance into the shafts. The thickness of the striations varies but most of them are fine and linear. Between the lines the bones may be porotic. Voorhoeve called attention to the appearance of both clear areas and dense spots in certain bones and he pointed out that in some places one of the dense lines appeared to break through the cortex. The striation may or may not extend into the adjacent epiphysis. Sometimes the epiphyses are mottled with dense and clear spots. Striation is well seen in the tarsus and especially the calcaneus.

Thus far, no pathological material has been available for investigation but it seems probable that the microscopic examination would reveal only normal bone of varying denisty. The differential diagnosis must be made from dyschondroplasia and osteopoikilosis. It is true that in osteopoikilosis the spots may be prolonged in some places into streaks but these are much shorter and much less regular than the dense lines seen in osteopathia striata. In Paget's disease an appearance worthy of the name of striation is exceptional except that in early stages of the disease it may be quite marked in the os calcis.

In the article on osteopathia striata, Fairbank includes a section on generalized hyperostosis with pachydermia. Among the cases published with roentgenograms, Fairbank was unable to find a single case that was strictly comparable with the patient reported first by Uehlinger. Two cases are discussed by Fairbank, one in which, however, there was no pachydermia. The roentgenographic changes were of two kinds: (1) coarse striations of cancellous bone, and (2) thickening of the cortices of long bones. The striation was much coarser than that seen in osteopathia striata, and it was seen particularly well in the metaphyses and epiphyses of the long bones, the

vertebrae and the tarsus. The hyperostosis which, on the whole, was more pronounced on the external than the internal surfaces of the cortices was seen on the shafts of all long bones. Some of the thickened bones were irregularly honeycombed, the appearance being rather suggestive of Paget's disease.—*R. S. Bromer, M.D.*

Lewis, K. M., Boutelle, W. E., and Roberts, M. A. Intracapsular fracture of the neck of the femur; observations on 152 patients treated by internal fixation with the Smith-Peterson nail. *Ann. Surg.*, March, 1950, *131*, 376–384.

The authors report a study of 152 consecutive patients with intracapsular fractures of the neck of the femur, treated from January, 1937, to January, 1948. All of the cases were treated by Smith-Petersen nail fixation, and all deaths or complications that occurred during the hospital stay are included.

The authors feel that great improvement has resulted with the use of internal fixation over the older methods of treatment of fractures of the neck of the femur. They feel that the Smith-Petersen nail is the ideal, in that it produces firm fixation, at the same time preventing rotation of the fragments. They believe that none of the screw methods is adequate.

Vitallium nails are used exclusively. One nail broke as the result of trauma. Only a small number of nails loosened and were extruded. The authors feel that the small number of such occurrences is due to the absence of ionization, which results in bone necrosis around the nail.

Internal fixation is used regardless of the age of the patient. The advanced age group withstands the procedure surprisingly well. In the winter of 1946–1947, 20 patients over eighty years of age with this fracture were operated upon, with only 2 postoperative deaths. The hips are not nailed as an emergency procedure.

The author gives in detail the routine procedure which he uses. Early ambulation is urged, and the patients are out of bed in a wheel chair within a few days. An ambulatory Thomas splint is then made for each patient, as unsupported weight bearing is not allowed for six months, or until roentgenograms clearly show bone trabeculations crossing the fracture line.

There were 12 deaths, or a mortality rate of 7.8 per cent. Most of these were due to poor general condition. There were 5 infections, or a rate of 3.2 per cent.

Of 106 patients who could be followed for at least a year, 79 patients, or 74 per cent, obtained union verified by roentgenograms, and were walking without support.

In this series late aseptic necrosis of the head of the femur has been very infrequent. Of the cases followed over three years, there have been patients who have this complication. The authors feel that important procedures to prevent late aseptic necrosis and non-union are: (1) a sufficiently long nail to reach well up into the head of the femur; (2) real impaction of the fragments.—*T. F. Wachowski, M.D.*

Burman, Michael, and Neustadt, Ernest. Torn discoid meniscus; association of discoid meniscus with congenitally high position of the fibular head. *Arch. Surg.*, Feb., 1950, *60*, 279–293.

The authors describe vividly the development of the fibula in lower animals. The embryological development of the fibula in humans is well portrayed with special reference to the relationship of the head of the fibula to the knee joint.

The variations in the relationship and development of the upper end of the fibula in man are set forth to help explain many of the torn meniscus.

Snapping of the knee joint and locking of this joint should presuppose a congenitally malformed external meniscus. The presence of a high fibular head is very rarely if ever reported clinically but is usually found on the roentgenogram. Three groups of cases are reported: (A) discoid meniscus without tear; (B) border line between snapping and locking of the joint; (C) tear of the discoid meniscus which locks the knee joint. The introduction of 50 cc. of air into the knee joint to better visualize the cartilage is an excellent suggestion. The roentgenographic signs suggesting discoid meniscus are: (1) flattening of the external femoral condyle; (2) widening of the joint space; (3) high fibular head.

The conjoined entity of discoid meniscus and high fibular head is likely to be less common than the entity of discoid meniscus alone. The discoid external meniscus is a congenital anomaly which may remain symptomless throughout life. It is the common cause of snapping knees in childhood and adolescence. If it tears it does not tear in the body of the meniscus but

at its anterolateral or posterolateral capsular origin, to give internal derangement of the knee, both in childhood and in adult life. The treatment is always surgical.—*L. S. House, M.D.*

BLOOD AND LYMPH SYSTEM

Buchman, Joseph. Sickle cell disease simulating osteomyelitis. *Bull. Hosp. Joint Dis.*, Oct., 1949, *10*, 239–251.

This is a report of a five year old negro female with sickle cell disease, giving a detailed account of the clinical course and laboratory findings. Three months after onset she complained of pain in the left leg. Roentgenograms revealed "a periostitis of the middle half of the fibula with areas of rarefaction and condensation of the involved portion of the shaft characteristic of sequestration and involucrum formation in pyogenic osteomyelitis." The author advised no treatment, surgical or antibiotic. The involved area regressed to practically normal bone in the course of two years. He explains this bone involvement on the basis of thrombosis and infarction, with aseptic necrosis. The question is raised as to the possibility that bone lesions are more frequent than reported and they are overlooked because of the mildness of the local symptoms and the spontaneous repair.—*F. H. Squire, M.D.*

Almklov, J. R., Hansen, A. E., and Schneider, M. D. Long bone involvement in sickle cell anemia. *Pediatrics*, Feb., 1950, *5*, 204–209.

Bone involvement in sickle cell anemia was not reported before 1924. Graham reported changes at that time in the long bones as seen at autopsy. In 1926 Cooley reported typical skull changes in the roentgenogram. In 1929 Moore reported roentgen changes in the long bones of a twenty-four year old male Negro. He described narrowing of the medullary cavity as a result of cortical thickening. Grinnan reported the first case of long bone changes in sickle cell anemia in a child. Caffey, in 1937, studied the long bones of 15 children with sickle cell anemia but found no evidence of long bone changes. In a study of 27 cases of the disease Diggs, Pulliam and King were able to demonstrate long bone changes in 11 cases, only 1 of which was a child.

The authors report the case of a twenty-one month old male Negro who sustained a pathological fracture of the femur. All the long bones showed multiple growth disturbance lines. The medullary cavity of each femur was greatly widened and showed evidence of old infarction. Films of the skull showed reduplication of the inner table of the frontal and facial bones. The chest films showed cardiac enlargement.

The congenital hemolytic anemias all show evidence of hyperplastic bone marrow. This leads to thinning of the cortex and widening of the medullary cavity. In addition, in sickle cell anemia, there is thrombosis of the blood vessels of the bone. This causes necrosis, hemorrhage, fibrosis, abnormal calcification and new bone formation. This takes the form of linear trabeculae adjacent to the cortex. On the roentgenogram the cortex is widened irregularly and the medullary cavity will be narrowed. Thus the roentgen appearance in sickle cell anemia depends on which pathological process is dominant, the hyperplasia of the marrow, which causes thin cortex and wide medullary cavity; or the vascular thromboses which lead to thickening of the cortex and thinning of the medullary cavity. The latter process is usually dominant in adults and the former in children.—*R. M. Harvey, M.D.*

Prouty, Margaret. Familial erythroblastic anemia in an American Indian infant. *Am. J. Dis Child.*, Jan., 1950, *79*, 99–104.

In this paper a case of anemia is reported resembling erythroblastic anemia (Cooley's anemia) in an American Indian infant, two and three-quarter months of age. It is of special interest because it is believed to be the first case of the condition reported in a person of this race and also because of the extremely early age at which the condition became apparent. The author suggests that it is increasingly evident that cases of familial erythroblastic anemia are overlooked because the attending physician fails to keep it in mind except when treating descendants of persons of the Mediterranean races.

The case presented a problem in diagnosis. At first the diagnosis of an obstructive jaundice was considered. Erythroblastosis fetalis also had to be ruled out and hemolytic jaundice also was excluded. The absence of splenomegaly and the severe jaundice could be explained on the basis of the patient's immaturity. Unfortunately, roentgenograms of the bones were not made.—*R. S. Bromer, M.D.*

VAN DER WERFF, J. Th. Long remissions in Hodgkin's disease. *Acta radiol.*, Jan., 1950, *33*, 31–40.

In 1832 Hodgkin described 7 cases in which there was painless swelling of lymph nodes, enlargement of the spleen, cachexia and fatal termination. We now know that all 7 of these patients did not suffer from the same disease but that probably 3 of them were the victims of the illness we now know as Hodgkin's disease (malignant granuloma or lymphogranulomatosis).

Concerning treatment of this disease there has been no unanimity of opinion. One is confused by the multitude of remedies advised. If one considers what has been achieved by all these various treatments one must conclude that, up to the present, treatment with the roentgen rays gives by far the best results. Yet even here there is no real agreement and the following various techniques are applied:

1. Local high voltage roentgen treatment in fractionated tissue destructive doses (O'Brien, Ratkóczy, etc.).

2. The same followed by irradiation of other fields were non-observable foci are expected (Gilbert, Jackson and Parker, etc.).

3. The same followed by general body irradiation (Medinger and Craver).

4. Local high voltage roentgen treatment in palliative doses (Slaughter and Craver).

5. Local moderately high voltage roentgen treatment in palliative doses (Desjardins).

6. General body irradiation (Marchal, Mallet and Bellin).

Classification into acute, subacute and protracted cases (O'Brien), in forms with slow evolution, rapid forms and acute forms (Gilbert) as well as into paragranuloma, Hodgkin's sarcoma and Hodgkin's granuloma (Parker and Jackson) remains subjective to a high degree. Consequently, statistics prove little as to the best mode of treatment.

The author has treated a group of 32 patients in his department. He concludes:

1. A long remission in his first patient was obtained by intensive penetrating irradiation and in his second case by a somewhat more moderate dosage, apparently due to extreme radiosensitivity.

2. The case record of the first patient makes it clear that pregnancy has no influence on the course of the disease.

3. To contradict the statement that during the remissions the blood picture and the sedimentation rate remain abnormal, two patients showed perfectly normal blood counts and sedimentation rates during their remissions.

4. One must admit this disease starts locally and then spreads metastatically.

5. Two of the author's cases are now enjoying six and five and a half year remissions respectively. It appears that all long remissions have been obtained by complete extirpation of the glands in very early cases or by application of intensive penetrating irradiation.—*Mary Frances Vastine, M.D.*

HAIMOVICI, HENRY. Gangrene of the extremities of venous origin; review of the literature with case reports. *Circulation*, Feb., 1950, *1*, 225–240.

This article calls attention to a rare but important cause of gangrene of the extremities, i.e. venous obstruction alone. This clinical condition is important because the proper treatment of the gangrene it causes depends upon the correct diagnosis. There are less than 30 cases reported in the literature of gangrene following extensive thrombophlebitis without arterial occlusion.

Historical data are reviewed. The clinical manifestations are summarized from 27 reported cases. The cases go through three typical stages: (1) phlegmasia alba dolens or milk leg; (2) phlegmasia caerulea dolens or blue thrombophlebitis, and (3) gangrene. Cyanosis is the most characteristic sign. This appears early, develops rapidly, and extends to the entire extremity. Pain constantly accompanies cyanosis.

The arterial system is patent as indicated by palpable pulse, oscillometric exploration, arteriography or postoperative or postmortem examination.

The author reports 2 new cases. The symptoms and differential diagnosis are given in detail. This is followed by a discussion of the pathologic physiology of the circulation of the extremities.

The treatment is conservative. Amputation is not required in the majority of cases.—*J. H. Harris, M.D.*

STARKLOFF, G. B., BRICKER, E. M., MCDONALD J. J., and LITZOW, L. T. Proximal femoral venography; preliminary report. *Ann. Surg.*, March, 1950, *131*, 413–417.

The authors present a preliminary report concerning an improved technique for roentgen examination of the deep veins of the lower extremity. They believe that thorough knowledge of these veins is essential to rational treatment of existing defects; and, since the usual type of phelebogram produces unusual pressure changes, the findings do not show the true physiology of the vessels involved.

In their procedure (which, they point out, is very similar to that developed by G. Bauer in 1948) the contrast medium is injected into the isolated, proximal saphenous stump with as as little pressure as possible. The injection and roentgenograms are made with the patient erect. Delay in emptying and amount of retrograde flow are of great significance. There is no detailed discussion of interpretation, but 4 cases are presented, with illustrations, to demonstrate the results to be expected.—*K. F. Kesmodel, Jr., M.D.*

Holden, William D. Reconstruction of the femoral artery for arteriosclerotic thrombosis. *Surgery*, March, 1950, *27*, 417–422.

The author presents 1 case of arteriosclerosis with thrombosis of the left femoral artery that showed considerable improvement following femoral artery reconstruction.

The patient, a male, aged forty-eight, was a known diabetic, and had had numerous previous hospital admissions for peripheral vascular disturbances. At the age of forty-seven he had a right supracondylar amputation for arteriosclerotic ischemic necrosis of the right foot. On his last admission he complained of swelling and tingling of the distal portion of the left foot and moderately severe, constant pain in the left heel. An arteriogram performed at that time by the injection of 20 cc. of 35 per cent diodrast into the common femoral artery demonstrated a segment of occlusion 8–10 cm. in length in the lower third of the artery. At surgery the occluded portion of the artery was resected, and a section of the saphenous vein was sutured in place of the resected artery. A posteroperative arteriogram showed an excellent flow of contrast material into the popliteal artery, as well as a marked reduction in the quantity of contrast material carried by the small collaterals evident in the preoperative arteriogram. The patient has been free of pain for 4½ months, and has demonstrated obvious signs of increased blood flow.

The author feels that a procedure of this nature, of necessity, must first be attempted on patients who are to have a thigh amputation. If successful outcomes can be obtained in these patients, he feels that femoral arteries that are the site of no more than moderate disease may be resected with anticipation of greater benefit. —*G. J. Culver, M.D.*

GENERAL

Soeur, R. La calcinose. (Calcinosis.) *Acta chir. belg.*, Feb., 1950, *49*, 240–248.

The total number of cases of so-called generalized calcinosis (a veritable petrifaction of the subcutaneous tissues) reported so far is about eighty. The author presents such a case and discusses it in detail.

Commenting on this rare clinical entity the author distinguishes three forms: (1) generalized interstitial calcinosis, (2) circumscribed calcinosis (pseudogout) which develops insidiously in contrast to real gout, (3) pseudotumoral calcinosis (described by Inclan in 1943) mainly in bursae and muscles. These three forms have certain common characteristics which are essentially the following: (a) calcareous and mineral deposits (and not bone formations) in the mesenchymatous tissues; (b) the skeletal system remains intact and normal; (c) calcium, phosphorus and phosphatase values of the blood are normal while occasionally there may be an increase in cholesterol and uric acid.—*J. N. Sarian, M.D.*

Peters, J. H., Horn, R. H., and Greenman, L. Idiopathic calcinosis universalis cutis without disability. *Ann. Int. Med.*, Jan., 1950, *32*, 138–145.

The authors present the case of a fifty-seven year old swarthy Mexican housewife, giving a five year history of a gradual development of multiple large lumps beneath the skin of her arms, legs, abdomen, ischial and gluteal areas. The lumps had increased in size and hardness without any associated subjective symptoms. For two years previous to the appearance of the nodules she had had muscle and joint pains in the extremities associated with swelling of the interphalangeal joints of the fingers. These symptoms had disappeared when the lumps were discovered and it was impossible to determine if this rheumatic episode represented the initial period of calcification.

Roentgen studies revealed some lumps to be discrete, others to be poorly defined and spotty in pattern, still others to be reticulated and of

vascular pattern. This case seemed to fall in the category of calcinosis universalis but strangely did lack symptomatology referable to the lesions. There was no change in the overlying skin. Biopsy of a hard lump revealed a stony calcific nodule. Microscopic section was typical of degenerative fatty connective tissue with large calcium deposits. Chemical analysis revealed 20.6 per cent calcium by weight. One para-umbilical mass proved to be a lipoma.

The patient sought medical relief for a loss of appetite, weakness, effort dypsnea and swollen ankles. She was found to have a large liver and spleen; myocardial weakness, probably of rheumatic etiology; and anemia. Blood chemistry studies revealed slight abnormality of serum protein fractions but no more than is naturally expected in liver disease. Serum calcium was 9.40 mg. per cent, serum phosphorus 3.45 mg. per cent, and unfilterable calcium 5.85 mg. per cent. Both negative and positive balanced and elevated blood calcium have been reported by others. The calcinosis feature of this case seems to fall in that group in which no accompanying or predisposing pathology can be detected.

This disease is often attributed to the breaking down of fat either as a result of trauma or too rapid loss of weight. Neither of these factors could be incriminated in this case. The possibility of such deposits occurring in reversible disturbances of serum calcium and phosphorus levels is discussed and mention made of transient renal insufficiency, overdose of vitamin D, exposure to excessive concentration of fluorides, impaired vascular integrity or other as yet unknown stimuli.

It is not clear why calcinosis should itself be non-reversible but often progress to a fatal termination after calcium and phosphorus balance had returned to normal. Efforts to control or arrest the progress of this condition is usually fruitless as is the case in most degenerative diseases of unknown etiology. The most remarkable feature of this case was the extensiveness of the involvement and the total absence of symptoms.—*Harold O. Brown, M.D.*

Lowe, C. E., Ellinger, A. J., Wright, W. S., and Stauffer, H. M. Pseudohypoparathyroidism (the Seabright bantam syndrome). *J. Pediat.*, Jan., 1950, *36*, 1–10.

Pseudohypoparathyroidism is a very rare disease. It is characterized by the presence of a slow serum calcium with a high serum inorganic phosphorus level; obesity with a rounded face; stubby fingers with a relatively long index finger, acalcification of tooth roots, and mental retardation. The most striking feature of the disease is failure of phosphate diuresis following intravenous administration of parathormone.

The name "Seabright bantam syndrome" was suggested for this entity by Albright because he felt it was a failure of end organ response (kidney) to parathormone. The Seabright bantam roosters have female tail feathers which presumably do not respond to male sex hormones.

The authors present a case in which insensitivity to parathyroid extract was present plus many of the clinical features which have been enumerated above. Their patient had had a life-long steatorrhea which they believe was the main etiological factor in the syndrome in their particular case. Large doses of vitamin D caused return to normal of the serum calcium and phosphorus levels. They postulate the following sequence of events: The primary disease was steatorrhea present since early life. This caused malabsorption of fat-soluble vitamins. Malabsorption of vitamin D led to failure of absorption of calcium from the intestinal tract causing hypocalcemia and tetany. Roentgen examination of the wrists at four months of age showed changes compatible with rickets. Prolonged parathyroid stimulation resulted from poor intake of milk, malabsorption of calcium and secondary hypocalcemia. They postulated that the kidneys became refractory to parathormone because of continued overstimulation. This phenomenon has been demonstrated in patients and experimental animals subject to prolonged administration of parathormone. Animals maintained on low-calcium diets rapidly become resistant to parathyroid extract.

In conclusion, the authors feel that some cases at least of the Seabright bantam syndrome may be due to chronic overstimulation of the renal tubules by the parathyroid gland with eventual failure of response of these end organs.—*R. M. Harvey, M.D.*

Wiener, L. R., and Richmond, J. B., The diagnosis of surgical conditions of the newborn infant. *J. Pediat.*, Jan., 1950, *36*, 107–121.

According to the 1947 United States Summary of Vital Statistics, congenital anomalies are second only to prematurity as a cause of neonatal deaths. Recent developments in sur-

gery which permit correction of many of these anomalies emphasize the importance of their early recognition and treatment.

The authors list the important clinical findings together with diagnostic methods employed in many surgical conditions of the newborn infant with reference to the gastrointestinal tract. Among the conditions discussed are atresias of the esophagus and intestines, intestinal stenosis, imperforate anus, malrotation of the intestines, diaphragmatic hernia, meconium ileus, intussusception, duplications of the alimentary tract, pyloric stenosis, and megacolon.

Roentgenologists who do not encounter these conditions frequently are urged to read the original article for a concise summary of the salient features of these conditions together with the important roentgen diagnostic findings.—*R. M. Harvey*, M.D.

Van Ordstrand, H. S., Netherton, E. W., De Nardi, Joseph M., and Carmody, Morris G. Beryllium skin granulomas from a broken fluorescent tube. *Cleveland Clin. Quart.*, Jan., 1950, *17*, 34–37.

The authors report a case of skin granuloma on several fingers, following laceration from a fluorescent lamp tube manufactured with beryllium phosphor. The histopathology is similar to that of the chronic pulmonary granulomatosis observed in persons exposed to beryllium. The granuloma is cured by local surgical excision.

Prevention of fluorescent lamp tube cuts is extremely important. They report that the fluorescent industry has discontinued the manufacture of tubes with beryllium phosphor, but many such tubes remain in use and in stock.—*A. A. Brewer, M.D.*

Dunphy, J. E. Some observations of the natural behavior of cancer in man. *New England J. Med.*, Feb. 2, 1950, *242*, 167–172.

It is generally accepted by surgeons that cancer grows in a steady and irrevocable manner, the rate of which is a function of the particular tumor and bears a fairly close relation to the histopathologic appearance of the lesion. Apparent arrests or regressions of tumors are usually attributed to faulty observations or to recent therapy, and little or no consideration is given to the possibility of a natural resistance to cancer. The thesis of this paper is that malignant neoplasms undergo periods of spontaneous arrest or regression alternating with periods of growth and that this phenomenon is, at least in part, a function of local tissue resistance.

To support the hypothesis that cancer may regress spontaneously, the author presents the case of a fifty-four year old woman who had an abdominal laparotomy on October 3, 1936, to remove a hard nodular mass in the pelvis. This mass involved the right adnexa and infiltrated the posterior surface of the uterus. Tumor nodules were scattered throughout the omentum. No metastases were seen or palpated in the liver. Complete removal of the mass was considered to be impossible. A biopsy proved the tumor to be a small round cell carcinoma.

During the next two years the patient had intermittent attacks of abdominal pain and was failing rather rapidly. In October, 1938, terminal care was arranged, but without specific therapy the patient suddenly began to improve. She continued to improve and did not return to the hospital until February, 1946. Then she was complaining of a mass in the right groin. This mass had appeared one year earlier and had slowly increased in size. Abdominal and pelvic examinations showed that the pelvic mass had disappeared and that the uterus was again movable. The lesion in the groin, an encapsulated mass of neoplastic nodes, was excised. Histopathologic examination proved that the nodes were heavily infiltrated with rapidly growing carcinoma. The cells were of the same type as the original tumor, but there was a papillary arrangement of the tumor. Two years later, in 1948, a nodule was removed from the right neck, but it proved to be a benign lipoma. In 1949 the patient was alive, well and apparently free of active neoplasm—thirteen years after the original inoperable pelvic tumor was discovered.

Clinical evidence for a natural resistance against cancer is only circumstantial. It can be inferred from the development of late recurrences, the regression or arrest of tumor in one site while it is progressing elsewhere, and the occasional explosive spread of cancer. To illustrate these points the author presents 3 case histories.

The first patient was a sixty-nine year old unmarried woman who entered the hospital in July, 1947, to have a cholecystectomy. She had had a radical mastectomy at another hospital in 1933 for cancer of the right breast.

There was no evidence of local recurrence of the neoplasm. During the operation to remove the gallbladder, an incidental appendectomy was done. Serial sections through the tip of the appendix revealed an unsuspected small metastatic focus. Histopathologically the cells in the appendix were consistent with a breast cancer. On the fourteenth postoperative day the patient had pain in the right chest and pleural effusion developed. Cancer cells were found in the fluid. Nine months later more fluid was removed from the right chest and again tumor cells were found. One year later fluid was again removed for study and no tumor cells were found. Two years following her operation (sixteen years after removal of the breast and two years after cancer cells were found in the pleural fluid) the patient was active and well except for moderate amount of fluid in the right chest.

The second case in this group was an example of the rapid growth of cancer at one site (ovary) while it remained dormant at another (liver). In November, 1946, a large, but easily resectable neoplasm was excised from the splenic flexure of the colon of a fifty-five year old woman, and an end-to-end anastomosis was done. There were several metastases in the liver. Eighteen months after the original operation the patient re-entered the hospital complaining of vaginal bleeding. The liver was slightly enlarged, and there was a mass filling the pelvis. The mass was considered to be a large ovarian tumor, and at operation proved to be a partially cystic adenocarcinoma of the left ovary. It measured 12 cm. in diameter and was excised along with the right ovary. The liver contained many nodules but its general size was not much different from what it was in 1946. The patient ran a slowly retrogressive course until her death in March, 1949.

The explosive spread of cancer was illustrated by the third case in the group. A fifty-nine year old Negro had a large palpable tumor in the right abdomen and a history of intermittent diarrhea for two years. At operation a right colectomy was done for a carcinoma of the ascending colon. The regional nodes were heavily infiltrated with tumor and there was seeding on the serosa of the ileum. The liver was small and apparently free of metastasis. Convalescence was uneventful, but the patient was dead within ten weeks of the operation with massive metastatic growth in the liver.

The author discusses the theoretical and practical significance of these observations.—*J. R. Hannan, M.D.*

Dargeon, Harold W., Eversole, Joseph W., and DelDuca, V. Malignant melanoma in an infant. *Cancer*, March, 1950, *3*, 229–306.

This is a case report of a nine month old male with a malignant melanoma which presumably arose by transplacental transmission.

The historical review which is included shows this condition to be rare.

A variety of malignant tumors have demonstrated metastasis to the placenta, and with infiltration into the intervillous spaces or in areas of infarction, the possibility of transference to the fetus is quite possible.

The patient presented a small mass in the external auditory canal which bled easily. It was thought to be granulomatous tissue but biopsy showed malignant growth of undetermined type. There was also malaise, a left-sided facial palsy, swelling anterior to the ear, and an enlarged lymph node below the ear. Roentgen studies were all negative.

An exploratory operation on the left mastoid revealed a black, shiny, soft mass which had, according to biopsy taken, infiltrated bone. At another hospital the preauricular node was removed and a diagnosis of malignant melanoma was made. Surgical removal was thought impossible and an extract of tumor tissue after receiving 800 r to the saline preparation and injected subcutaneously was of no benefit. The patient died three months after onset of symptoms.

Autopsy showed dissemination of the malignant process with chief involvement in the liver and lungs.

The family history is particularly pertinent as the child's mother had a malignant melanoma of her leg. She died four days after the cesarean delivery of this infant. Autopsy revealed widespread metastatic involvement of most visceral organs including the uterus.

This seems to establish the transplacental transmission of the malignant process from the mother to the infant.—*John S. Scott, M.D.*

Squires, A. H., Kofman, O., and Cunningham, J. N. Adult Gaucher's disease. *Canad. M. A. J.*, Feb., 1950, *62*, 178–181.

A case of adult Gaucher's disease with acute pericarditis with effusion and substernal and shoulder pain is reported. This type of pain and pericarditis with effusion has not been pre-

viously reported as an association with Gaucher's disease. The patient was a twenty-four year old, non-Hebrew, male, with no hereditary or familial tendency for this disease. The diagnosis was made from a sternal puncture, the marrow showing many typical Gaucher cells described as variable in size, being from 30 to 40 microns in diameter. They possessed one to two small, darkly stained, eccentrically placed nuclei. The pale cytoplasm was abundant and contained concentric fibrils about the nuclei. This patient presented some of the commonly described features of the disease, viz., large spleen and liver, leukopenia, brown discoloration of the skin and changes in the humeri, tibiae and femora as shown roentgenographically. The lower ends of the femora were slightly expanded, the cortex thinned and the medullary canal osteoporotic with areas of sclerosis of the medullary portion in several locations. Some features of typical Gaucher's disease, such as pingueculae of the subconjunctivae, thrombocytopenia and hypochromic anemia were not present in this case.

Gaucher's disease is a rare condition, often familial, distinguished by the presence of characteristic cells in the organs of the reticuloendothelial system and occurring usually during the first decade of life. The disease is considered to be a manifestation of a disturbance of lipoid metabolism involving the cerebroside known as cerasin. The relationship of pericarditis with Gaucher's disease is obscure but the shoulder and substernal pain may be explained on the basis of the pericarditis and the marrow infiltration by the Gaucher cells. No specific therapy is known. Splenectomy is advised when there are local abdominal symptoms due to splenomegaly and when there is a hemorrhagic tendency. The need for marrow studies in similar cases is stressed.—*W. L. Kilby, M.D.*

Fairbank, H. A. Thomas. Myositis ossificans progressiva. Synonyms—fibrositis ossificans progressiva. *J. Bone & Joint Surg.*, Feb., 1950, *32B*, 108–116.

Myositis ossificans progressiva is a congenital affection characterized by the formation of columns of bone in the soft tissues with progressive limitation of movement. It is usually associated with microdactyly. There is little evidence of hereditary or familial influence. The title is unfortunate because the primary change is in the connective tissues, fasciae and tendons, the muscle fibers being affected only secondarily and moreover the changes are not of an inflammatory type. Both sexes are affected, males more often than females. The microdactyly arises in fetal life, but the other manifestations usually develop in childhood before the age of ten years.

Maldevelopment of the great toe arises in fetal life, and the fault that is responsible for changes in the muscles, no matter how long their onset is delayed, is also congenital. No cause of this mesodermal fault is known. No error in calcium metabolism has been proved.

Severe crippling may supervene within a few years or it may be delayed for three or four decades. Localized swellings appear during infancy and childhood, usually in the region of the head or neck and sooner or later in the trunk. Injury may sometimes determine site of a lesion and start the whole process, but, as a rule, injury plays no part at all. Sooner or later columns, irregular masses or plates of bone appear in the soft tissues. If a lump does not disappear completely bone may be expected to make its appearance within a period of from two to eight months. These bony columns seem to lie in the course of a muscle. Certain muscles seem to be exempt, namely the muscles of the eye, face, tongue, diaphragm, heart, larynx, perineum and the sphincters. Bone formation has seldom occurred in the skin or in the abdominal wall.

In regard to the microdactyly, the great toes are affected in about three-quarters of all cases. Hallux valgus is common and there may be a scar over the metatarsal head. Reduction in the length of the thumb is less frequent; it occurs in only half of the cases.

Roentgenograms show a varying degree of density of the extraskeletal bone. Exostotic projections or subperiosteal thickenings on the shaft of a bone may be seen in addition to columns of bone in the soft tissues. In an advanced case there may be fusion of vertebrae. Microdactyly is usually associated with reduced length of the phalanges of the great toe and only exceptionally with a short metatarsal bone. There is complete or incomplete suppression of the proximal phalanx which may be reduced to a wedge-shaped fragment. The first metatarsal may actually be increased in length by fusion of part of the proximal phalanx, thus forming a rounded end to the bone quite unlike the normal head. In the thumb

all three bones may be short, or there may be shortening only of the phalanges.

The condition usually becomes progressively worse, but the rate of progress varies. Intermissions are not uncommon and sometimes there may be arrest for several years. No treatment is known to arrest the progress of the disease although the possibilities of radiotherapy, the author states, have not been fully explored. Operative excision of a bony column is very uncertain in its results.

The article is illustrated with roentgenograms of a case together with microphotographs of biopsy specimens and clinical photographs. Two line drawings of skeletons of museum specimens are also included. The sections on the clinical sign and differential diagnosis of the condition are especially complete.—*R. S. Bromer, M.D.*

Dyke, W. J. C., Hind, H. G., Riding, D., and Shaw, G. E. Bacterial synthesis of vitamin B_{12} in the alimentary tract. *Lancet*, March 18, 1950, *1*, 486–488.

It is becoming generally recognized that a breakdown in the normal metabolism of an essential anti-pernicious anemia factor—vitamin B_{12}—is the primary cause of pernicious anemia. It is therefore important to consider the sources from which normal man and animals derive this vitamin. Vitamin B_{12} is identical with, or closely allied to, animal protein factor, cow-dung factor and extrinsic factor. Vitamin B_{12} (extrinsic factor) may be derived from the diet or be produced by bacterial synthesis in the intestine. The vitamin B_{12} in the contents of the alimentary canal of a man, a horse and a sheep was assayed. Its amount was shown to be greatest below the ileocecal valve.

To confirm that the substance isolated from intestinal content was indeed an anti-pernicious anemia factor, some of the purified fractions were applied to the treatment of typical cases of pernicious anemia in relapse. The results of one such trial on 3 cases indicate that the material is clinically active when injected intramuscularly. The vitamin B_{12} content of the diet in the horse's daily intake is only a minute fraction of the daily excretion. Synthesis must therefore take place in the horse's intestinal tract, and work now in progress indicates that certain strains of lactobacilli isolated from the intestinal contents are capable of producing considerable amounts of vitamin B_{12}. Broadly speaking, synthesis is greatest in ruminants, somewhat less in equines, and definitely less in man. Nevertheless in man it seems that intestinal synthesis contributes the major portion of the total amount of extrinsic factor. Some advantage is undoubtedly to be gained by supplementing this with foodstuffs rich in vitamin B_{12}.—*S. G. Henderson, M.D.*

Hermann, Jack. Sarcomatous transformation in multiple neurofibromatosis (von Recklinghausen's disease); report of four cases. *Ann. Surg.*, Feb., 1950, *131*, 206–217.

The author presents an excellent review and summary of multiple neurofibromatosis (von Recklinghausen's disease) stressing the clinical, pathological and familial aspects of this condition.

The most serious complication of von Recklinghausen's disease is malignant transformation of a sarcomatous nature. The author presents 4 cases all suffering with this disease. Three cases developed sarcomatous changes in the sciatic nerves and the fourth case had retroperitoneal sarcoma. Metastasis from sarcomatous neurofibromatosis is usually late, but the lungs are the most common site of metastases. Regional lymph nodes are frequently involved. The only adequate treatment is wide surgical excision. Conservative surgical removal or biopsy of suspicious lesions is felt by the authors to predispose to sarcomatous change and early metastases. As a rule, sudden changes in the size of individual tumors occur at or about puberty and during pregnancy, at which times one must be especially watchful for sarcomatous manifestations.—*C. L. Hinkel, M.D.*

RADIATION THERAPY

Warren, Shields, and Bowers, John Z. The acute radiation syndrome in man. *Ann. Int. Med.*, Feb., 1950, *32*, 207–216.

In view of the present interest in atomic radiation and its effects upon human beings, this is an article which should be read in its entirety because it is a summation of present knowledge, presented clearly and concisely.

The syndrome of acute radiation in man consists of the sequelae which result from passage of gamma rays and neutrons through the body

of an individual, either following the explosion of an atomic bomb or when radioactive elements become distributed through the body by assimilation. Damage to tissues depends on their inherent sensitivity to radiation, and within the tissues themselves, sensitivity depends on the phase of mitotic activity. There is also a considerable variation within species. as is exemplified by response to an injurious dose of radiation accidentally received by three cyclotron workers; one man showed a pronounced fall in the white blood cell count, another only a mild reaction, and the third showed no change.

There is difference of opinion regarding pathogenesis of the syndrome. Some consider that the degree of hydration of cells is closely related to their sensitivity, the edematous cell being most sensitive. Some consider that the production of ion pairs within the sensitive structure produces the characteristic change. Others have shown that those enzymes which contain sulfhydryl groups are easily inactivated by ionizing radiation and may be reactivated by the introduction of reducing agents, which contain sulfhydryl groups. Some of the injurious effects of ionizing radiation have been attributed to formation of hydrogen peroxide in the tissues and, this theory is supported by the fact that cysteine and glutathione have been shown to exert a protective effect in animals. These substances are of no value in treatment after exposure to excessive amounts of radiation.

Studies of the Japanese casualties showed early disappearance of all blood-forming elements from the bone marrow, except scattered areas of erythropoiesis. By the end of the second week, the proliferating reticulum differentiated sufficiently to form lymphocytes and plasma cells, and in the fourth week myeloid differentiation was apparent. The marrow later showed hyperplasia with maturation arrest which finally disappeared. Lymphocytes disappeared from the lymphoid tissue by the third day and returned slowly, but at the end of three months were still reduced in number. As early as the fourth day the testes showed extensive necrosis of the germ cells, with subsequent hyalinization. The ovaries showed less striking changes, characterized by absence of corpora lutea. The gastrointestinal tract showed early and pronounced changes with mucosal edema extending into the submucosa, pseudomembrane formation associated with extensive ulcerative changes.

Total body irradiation causes a rapid and pronounced fall in the blood platelets, damage to the vessel walls, and the appearance of a circulating anticoagulant, resembling heparin. There is increased capillary fragility, followed by thrombopenia and appearance of the anticoagulant, with purpurae and petechiae resulting from these changes, appearing from four to seven days after the initial injury. There may be associated bleeding from the body orifices, these manifestations reaching their peak between the sixteenth and twenty-second day. Mucosal ulcerations develop in the gastrointestinal tract, resulting in diarrhea, the stools at first liquid, subsequently blood streaked, or bloody. The debrided gastrointestinal mucosa permits entry of organisms into the circulating blood stream. Asthenia is marked in the premonitory stages and subsequently is in proportion to the signs and symptoms, particularly of diarrhea and anemia. Nausea and vomiting are pronounced during the premonitory stage and may reappear subsequently with considerable severity. Epilation of hair of the scalp appeared about two weeks after exposure and in all individuals who survived, the hair re-grew and had the same texture and color as the original.

In fulminating cases, nausea, vomiting, prostration and mild diarrhea commence within two to six hours after exposure, gradually increase in severity and are associated with a pronounced fall in the white blood cell count. Diarrhea becomes increasingly severe, there is a step-like rise in fever, and death occurs from the fifth to the tenth day.

The hemorrhagic form shows initial nausea, vomiting, prostration, and, at times, mild diarrhea of about two days' duration. This is followed by a well period of about five days, which is followed by profound prostration, bloody diarrhea and increasing fever. Petechiae and purpurae appear and are associated with bleeding from body orifices. Ulcerative lesions of mucosal surfaces become increasingly extensive and death may occur from three to six weeks after exposure. Patients in this group have received irradiation by doses in the lethal or near lethal range.

Cases which survive for six weeks show pronounced anemia, reaching in levels as low as 800,000 to 900,000 red blood cells per cubic

millimeter. The white blood cell count usually reached levels less than 1,500 per cubic millimeter and recovery was rare in patients whose count dropped below 600. In the less severely injured cases, anemia often becomes the most pronounced finding.

Pronounced hypospermia or azospermia was found in a group of Japanese men examined ten weeks after the explosions. In many of the individuals the sperm count returned to normal over a period of from six months onward. A number of Japanese with the subacute type of involvement developed lung abscesses and others developed miliary tuberculosis.

Permanent sequelae have not been observed among the Japanese casualties. These studies are continuing and involve, among other things, searching for evidence of genetic changes in the survivors, possibility of late neoplasia, and subsequent appearance of blood dyscrasias.

Treatment is supportive and nonspecific. Liberal and repeated transfusions of fresh blood are useful. It is claimed that protamine, toluidine blue and rutin, have resulted in significant reduction of mortality in irradiated dogs, but there has been no opportunity to study these measures in man. Parenteral therapy is of great importance to restore salt and water lost by the bowel as well as to correct aberrations in blood electrolytes. Antibiotics should be used to combat infection. It is claimed that adrenal cortical hormones alleviate nausea, vomiting and prostration and it may be that the salt retaining properties of these hormones might prove helpful.

In the Hiroshima and Nagasaki explosions, 60 per cent of the deaths were due to trauma, 30 per cent to burns, and only 10 to 20 per cent to irradiation; it is apparent that many individuals succumbed to trauma or burns before the ionizing radiation syndrome had developed.

Regarding prognosis, patients who developed the fulminating course received amounts of radiation far in excess of the minimal lethal dose. Those exhibiting the hemorrhagic and pancytopenic forms received doses at or below the lethal range, and it should be anticipated that a number of the patients in this group would be salvaged. "Since the patients in the hemorrhagic and pancytopenic groups also exhibit a well period between the premonitory phase and the development of the full blown clinical picture, this occurrence should be looked on as a favorable sign."—*A. K. Wilson, M.D.*

Andersen, S. Ry. Differentiation and irradiation. *Acta radiol.*, Jan., 1950, *33*, 57–68.

During the half century that roentgen rays and radium have been used in the treatment of cancer the question has been raised repeatedly as to whether these rays possess a power to induce increased differentiation in malignant tumors and whether their curative effect might be partly or wholly due to this mode of action.

In conducting his investigations the author examined a number of characteristic types of tumors which, theoretically, should have the possibility of exhibiting histologically demonstrable differentiation before, during and after irradiation.

In none of the material did the author find any case which showed any sign of increased regular orderly differentiation (in the irradiated tumors). For example, in the squamous cell carcinoma in mice, theoretically differentiation should be particularly easy to induce because this tumor was originally a highly differentiated cornifying carcinoma. During continued transplantation its differentiation was considerably reduced and arrived at a fairly constant, low degree. A preserved capacity for further differentiation could, however, be seen from the frequent finding of traces of specialization in the otherwise undifferentiated tumor (in the form of parakeratosis and cornification with parakeratotic and horny pearls) and from the marked differentiation occurring in places in some of the controls.—*Mary Frances Vastine, M.D.*

Lahm, W. Zur biologischen Dosierung der Röntgenstrahlen und die Röntgenbehandlung funktioneller Störungen. (The biologic dosage of roentgen rays and roentgen therapy of functional disorders.) *Strahlentherapie*, 1950, *81*, 425–438.

This article, which is dedicated to Professor Alfred Stühmer on the occasion of the anniversary of his sixth-fifth birthday, deals in considerable detail with various problems which in fact reflect on the present-day status of roentgen therapy in general. As the title indicates, special emphasis is laid, however, on the problems of biologic dosage and treatment of the functional disorders by roentgen rays.

In regard to the first problem, the author states that the specification of a clinical dose of roentgen rays in the physical unit of the roent-

gen, although valuable from the point of view of determining the equivalent dose, is not sufficient to accurately express the biologic effect and thus render the biologic dosage, as the clinician knows it, unnecessary. On the contrary, the protraction of the treatment, the fractionation of the dose and the requirement of adjusting the dose to the general condition of the patient are factors which make an urgent introduction of a biologic dose unit desirable. Kepp suggested the so-called "biologic erythema dose" and the author is of the opinion that the size of this dose should be calculated in every case by taking into consideration the intensity of the roentgen beam, the fraction of the dose and the duration of the protraction. He distinguishes between two basic units of the biologic dose, the SED I (skin erythema dose) which corresponds to the ordinary skin erythema produced by 600 r in one seance by deep roentgen rays and the SED II which is the equivalent of the epidermolytic dose and is taken by the author to represent 1,300 r when given in one seance at an intensity of 42 r per minute.

To facilitate the clinical use of the biologic dosage based on these two units the author has elaborated a practical table which is reproduced in the text. He has plotted on the abscissa the r/min. values from 30–1 r, the fractionation with 5–20 exposures and the fractionation with 10–25 exposures. On the ordinate are the total dose in r for SED I (600 r and 800 r respectively), SED II (1,750 r) and the tolerance dose (3,800 r). If, for example, by using the technique for SED II a dose of 4,500 r was given in 15 fractions (instead of the dose of 4,200 r as indicated on the table) there was an overdosage of 7 per cent; in other words, a dose of 107 per cent SED II was administered.

In discussing the second problem, that is, the roentgen therapy of functional disorders, the author states that on the basis of above described biologic dose system he places all conditions treated by deep roentgen therapy into three groups: (A) mild irradiation with doses of 3–20 per cent SED I, at intervals of 1–10 days, for 3–6 treatments and a total dose up to ½ SED I. This group includes acute and subacute infections, various forms of tuberculosis, actinomycosis, lymphatic leukemia, hemangioma, warts, etc; (B) medium irradiation with doses of 20–50 per cent SED I, at intervals of 3–10 days, for 3–6 treatments and a total dose of 100 per cent SED I. This group includes many chronic infections, diseases of the hemopoietic system, chronic degenerative changes, all of the functional and endocrine disorders and a large variety of other conditions; (C) intensive irradiation with doses of 30–70 per cent SED I given every day or every other day for a total of 6–30 fractions and a total dose of 100–125 per cent SED II. In this group belong seminoma, lympho-epithelioma, recurrent lymphogranulomatosis, pituitary adenoma, glioma and all malignant tumors.

After reviewing the various theories of the mode of action of the roentgen rays and the results obtained in the functional and endocrine disorders (group B) the author draws the following conclusions: (1) it is possible to influence the disturbed neuro-endocrine regulation by roentgen therapy; (2) the dose must be small even in case of longer protraction; (3) not more than three series should be given within one year, and (4) very neurotic patients, as a rule, respond poorly to the irradiation.—*T. Leucutia, M.D.*

O'Brien, Frederick W. Roentgen therapy and the relief of pain. *Radiology*, Jan., 1950, *54*, 1–9.

This is a very interesting discussion of the causes of a phenomenon long recognized by radiation therapists. The author points out that the obvious explanation of the relief of pain following irradiation in boils and carbuncles lies in the relief of the tension in the tissues caused by stretching of the skin secondary to inflammation associated with inflammatory exudate. The cause of pain is considered in its relation to the explanation for the relief of pain.

The mechanism of the relief of pain in a number of conditions is discussed. These include the well known relief obtained in calcification of the supraspinatus tendon, herpes zoster, Marie-Strümpell spondylitis, other types of arthritis, and in metastatic bone lesions. It is pointed out that we should not wait for roentgen evidence of bone metastasis, for it is notorious that the spinal column and cord may be riddled with metastatic deposits not demonstrable by careful roentgen examination. It cannot be too strongly emphasized that a patient complaining of skeletal pain following an operation for a primary metastasizing neoplasm should have roentgen therapy irrespective of "negative" roentgenograms.

As one discussant of this paper commented, it is particularly interesting to get back to such a basic clinical consideration as the relief of pain, in these days when so much interest is centered around atoms, neutrons, electronic bombardment, isotopes, etc.—*D. S. Kellogg, M.D.*

Grau, E. Ergebnisse und Erfahrungen bei der Strahlenbehandlung kavernöser Haemangiome. (Results and experiences in radiation therapy of cavernous hemangiomas.) *Strahlentherapie*, 1950, *81*, 411–418.

This article is dedicated to Professor Alfred Stühmer on the sixty-fifth anniversary of his birth.

The author discusses his experience with the radium and contact therapy in a series of 320 cases of hemangiomas seen at the Dermatologic Clinic of the University of Freiburg from 1946 until the fall of 1949. The nevi flammei are not included. A follow-up was planned in 249 cases; of these 101 were treated by radium application, 135 by contact roentgen therapy and 13 by a combination of both methods. By omitting those cases which have not as yet been returned for final check-up examination and those which have been treated too recently, the series is narrowed to 108 cases, of which 42 received radium treatment, 55 contact roentgen therapy and 11 a combination of both.

The radium treatment was carried out with a 2 by 2 cm. plaque containing 16.9 mg. radium filtered with 1 mm. monel, usually applied at a distance of 0.5 cm. Its output was determined by the *Drosophila* method. A dose of 1,000 r was given divided into three fractions of 333 r each on successive days. In some instances the treatment was repeated by administering two or three similar fractions occasionally three and mostly six months later.

The Chaoul apparatus (60 Kv., 0.15 mm. Cu inherent filter) and the Philips apparatus (50 kv., 0.2 mm. Al inherent filter) were used for the contact roentgen therapy. The cutaneous hemangiomas were treated exclusively with the Philips apparatus at the 2 cm. skin focus distance, no filter or 1 mm. Al filter. The advantages of this apparatus are that the relative depth dose is exceedingly small, the exposure is very short and thus it can be applied very conveniently in children. For the larger cutaneous, subcutaneous and the cavernous subcutaneous hemangiomas the Chaoul apparatus with a skin focus distance of 5 cm. proved more efficient. The average dose in all cases amounted to 500 r (occasionally 250 r and in the small flat lesions 800 r). The treatment not infrequently was repeated in two to three months and at gradually spaced intervals for a total of three to four exposures.

The case histories of 6 patients are presented in brief résumés, including some photographs before and after treatment.

Comparative analysis shows that the results obtained by contact roentgen therapy equal those obtained by radium therapy. In view of the fact that contact roentgen therapy only requires a few minutes, it is generally preferred to radium therapy. Long intervals between treatments are essential to avoid late changes of the skin and thus to secure the best cosmetic effect. —*T. Leucutia, M.D.*

Zeman, Wolfgang. Die Toleranzdosis des Hirngewebes bei der Röntgentiefenbestrahlung. (The tolerance dose of the brain tissue to deep roentgen irradiation.) *Strahlentherapie*, 1950, *81*, 549–556.

Pennybaker and Russell in 1948 reported 5 cases of necrosis of the brain tissue produced by roentgen irradiation of the skull. Although such damage may depend on various constitutional factors, the author is convinced that there is a tolerance dose of the brain tissue which can be administered without inducing any anatomic changes. In the present article he estimates the size of this dose as it applies to the brain tissue of adults under well established conditions.

The problem is considerably complicated by the fact that different authors described different histopathologic alterations. The early reactions, which are usually of temporary duration and produce no clinical symptoms are difficult to observe. Greater benefit is derived from a study of the late changes appearing after a latent period of several months or years since they constitute the morphologic substratum of progressive lesions of the central nervous system often terminating in death. The author uses the term "radiation encephalopathy" to designate this anatomically as well as clinically demonstrable damage which he makes the basis of his study in evaluating the tolerance dose of the brain tissue.

Numerous animal experiments have been carried out through the years to determine the dependence of the late damage on the magnitude of the dose. By using deep roentgen rays

in rhesus monkeys, alterations of the brain tissues were obtained with single doses of 2,000–3,000 r. Russell, Wilson and Tansley in 1949 irradiated the brains of two groups of rabbits with 200 kv. corresponding to a half-value layer of 0.95 mm. Cu, and obtained routine radiation encephalopathy 100 days after the exposure when a single dose of 2,850 r was given and 240 days after the exposure when a single dose of 2,430 r was given, whereas from single doses of 2,030 r and 1,650 r respectively no clinical or anatomic changes were noted after two years. It is interesting that an increase of only 17 per cent (410 r) in the dose resulted in a 60 per cent (140 days) shortening of the latent period. The author believes that if the latent period is plotted on the abscissa and the dose on the ordinate of a coordinate system the resulting curve will assume an exponential character.

The task of applying the findings of animal experiments to humans is fraught with insurmountable difficulties. On the other hand, only a few individual cases of radiation encephalopathy following clinical roentgen therapy are described in the literature.

On the basis of 7 personal cases of brain tumor which were treated according to Köhler's method of pendulum irradiation, the author established the value of the tolerance dose of the human brain as being 5,300–6,000 r, under the following conditions: 180 kv., rotating tube, 7–26 r/min., fractions of 230–260 r on the lesion (focal dose), given 5–6 times per week. This dose corresponds in its biologic effect to a skin erythema dose (SED) of 130–150 per cent administered in one seance.—*T. Leucutia, M.D.*

Anzilotti, Alberto. Le indicazioni cliniché, i risultati e la tecnica dell'irradiazione funzionale diencefalo-ipofisaria. (The clinical indications, the results and the technique of the functional irradiation of the diencephalic hypophyseal region.) *Radiol. med.*, Feb., 1950, *36*, 129–137.

Roentgen therapy of the diencephalic hypophyseal region has been advocated for many different types of endocrine disturbances.

In a careful study of 200 cases, treated by irradiation of this region, the author concludes that favorable results are only obtained in those syndromes in which there is a definite dysfunction of the diencephalic hypophyseal system.

He stresses the necessity of a careful investigation of each case with full cooperation between the radiologist and internist and individual determination of radiation dosage.

He classifies the indications for irradiation of the diencephalic hypophyseal system as follows:

1. Hyperthyroid syndromes.
   Roentgen therapy of the pituitary region alone, or associated with irradiation of the thyroid gland and of the sympathetic system, is indicated in
   - A. Hyperthyroidism of the preclimacteric period or of the older female patients.
   - B. Hyperthyroidism of the gravidic and of the post-partum types.
   - C. Hyperthyroidism of puberty.
   - D. Hyperthyroidism which has not responded to irradiation of the thyroid gland.
   - E. Dysfunctions of the sympathetic system following thyroidectomy.
2. Essential hypertension.
   Although no cure is to be expected, the palliative effects obtained in selected cases may be superior to those resulting from other therapeutic measures. Roentgen treatment should be limited to those cases which have a diencephalic hypophyseal dysfunction.
   - A. Menopausal syndromes, with hyperglycemia and cephalalgia frequently associated with hyperostosis frontalis interna.
   - B. Hyperthyroidism in older female patients.
   - C. Hypertension of the climacterium, of diabetes and of hyperthyroidism.
   - D. In the essential hypertension of the male, the author did not obtain favorable results. He advises irradiation of the lateral cervical regions and of the suprarenals.
3. Dysfunctions of the female genital sphere.
   - A. Menopause, both physiological and artificial.
   - B. Dysmenorrhea and metrorrhagia of puberty and of the adult.
   - C. Primary amenorrhea.
   - D. Secondary amenorrhea.
4. Disturbances of the carbohydrate metabolism.
   Radiation therapy is *not* indicated in
   - a. Ordinary diabetes mellitus.
   - b. In the hyperglycemia and glycosuria of nephropathies
   - c. In the hyperglycemia and glycosuria of infectious diseases.
   - d. In the glycosuria of hepatic origin.
   - e. In renal diabetes.
   - f. In hypoglycemia.

   Radiation therapy *is* indicated
   - a. In the hyperglycemia without glycosuria of the hypertensive.
   - b. In the diabetes of advanced age (hypertensive and insulin resistant).

c. Hyperglycemia with hypersensitivity to insulin.
d. Pituitary hyperglycemia during pregnancy and immediately post-partum.
e. In the pituitary hyperglycemia with growth disorders and genital insufficiency.
f. In the glycosuria and hyperglycemia of the hyperthyroids which are insulin resistant.
g. In the glycosuria of pituitary adenomas.

—*A. A. Blasi, M.D.*

Vogt, Alfred. Die kombinierte Röntgen-Radium-Behandlung des Speiseröhrencarcinoms. Die Bedeutung der Schleimhautdiagnostik des Oesophaguscarcinoms für die Art des strahlentherapeutischen Vorgehens. (The combined roentgen-radium treatment of esophageal carcinoma. The significance of the relief diagnosis of esophageal carcinoma as regards the radiotherapeutic procedure.) *Strahlentherapie*, 1950, *81*, 439–458.

On the occasion of the sixty-fifth birthday of Professor Alfred Stühmer, to whom this article is dedicated, the author reviewed the combined method of external roentgen therapy and intraluminal radium application which has been used for years at Tübingen for the treatment of carcinoma of the esophagus and which was described by Schultz in 1938.

External roentgen therapy is administered through multiple small fields arranged in such fashion that the beam is limited to the site of the carcinoma and its immediate vicinity. In case of elongated lesions two rows of fields are used, the one crossfired for the upper part and the other for the lower part of the carcinoma. Irradiation of the heart is avoided and the spinal cord is protected by a strip of lead rubber. The technical factors are as follows: 180 kv., 0.5 mm. Cu filter, 40 cm. skin-focus distance, 200 r per field, 12–16 fields of 6 by 8 cm., the number of fields treated daily varying between 2 and 5 depending on the blood count and general condition of the patient. The response of the carcinoma is controlled by roentgen relief studies performed every ten to fourteen days. In case of rapid regression, and especially when the leukocyte count and the sedimentation rate indicate a marked disintegration of the tumor threatening a perforation of the esophagus, the focal dose is reduced. In the presence of an increased sedimentation rate intensive penicillin therapy is advisable even when the leukocyte count appears normal. In the average case the total surface dose amounts to 25,000 r given in eight to fourteen weeks but a dose as high as 35,000 r is not unusual. The individual field, as a rule, does not receive more than 3,000 r. This average technique is modified when the carcinoma is located at either end of the esophagus. The modifications are described in considerable detail.

The radium is applied at the conclusion of the transcutaneous roentgen irradiation, when the relief study indicates that the crater has disappeared. A radium sound 6 mm. in diameter is used and a dose of 3,000 gamma roentgens is given in contact with the sound. Three weeks later a second radium application is made and an additional dose of 1,500 gamma roentgens is given. In case that a stenosis of the esophagus develops a careful dilatation by following Starck's procedure is undertaken.

The combined focal dose from the roentgen and radium irradiation is very high. The author estimates that by making the necessary correction for the longer protraction it exceeds the tumor dose of 5,000–6,000 r delivered in thirty to forty days by the rotational roentgen therapy of Krebs which is recognized as the best method available at the present for the treatment of esophageal carcinoma.—*T. Leucutia, M.D.*

Schenck, Samuel G. Hidradenitis suppurativa axillaris; an analysis of 54 cases treated with roentgen rays. *Radiology*, Jan., 1950, *54*, 74–77.

Hidradenitis suppurativa axillaris, a persistent painful staphylococcal infection of the apocrine glands of the axilla, responds well to roentgen therapy, which the author considers the treatment of choice. Fifty-eight patients were treated, 54 of whom were followed for three months after therapy. Each patient improved after roentgen therapy, without recurrence, and without surgical procedure beyond simple incision of fluctuant abscesses.

Before institution of therapy, the axilla is shaved or the hair closely cropped. The author used technical factors of 180 kv. (peak) and an added filter of 0.5 mm. copper and 1.0 mm. aluminum, the radiation having a half-value layer of 0.9 mm. copper. A 10 by 10 cm. cone was used at 50 cm. distance, directly into the base of the axilla. A dose of 100 r per treatment is delivered in the acute stage, increasing to 150

to 200 r per treatment as the severity diminishes. Treatments are given three times a week for five to ten treatments, to a total of 1,000 to 1,200 r (air). In the author's 54 cases with follow-up, an average of 7.8 treatments was given to cure each axilla.—*H. P. Brean, M.D.*

Ott, Paul. Röntgentiefentherapie des Bronchialkrebses in Verbindung mit Progynon C-Behandlung. (Deep roentgen therapy of bronchial cancer in association with progynon C treatment.) *Strahlentherapie*, 1950, *81*, 584–586.

Statistical analyses furnish undoubted proof that bronchogenic carcinoma is constantly increasing in frequency. In Berlin, the author has observed since 1945 more cases of bronchogenic carcinoma than of cancer of the stomach, whereas formerly the opposite was true. It is significant that this increase occurred at a faster rate in the male than in the female. Thus Lubarsch in 1924, on the basis of 450 cases autopsied at Charité, found a ratio of 3:1 between bronchogenic carcinoma of the male and that of the female. In the author's series of 143 cases, seen during the past twenty years, this proportion widened to 7:1 in the histopathologically proved group and to 11:1 in the entire group. The author, therefore, is of the opinion that bronchogenic carcinoma is a disease predominantly of the male sex which during the past years has shown a marked increase in the relative ratio.

The situation is similar to that observed in cancer of the larynx which is known to affect the male sex twenty times as frequently as the female sex. Embryologic and developmental factors, such as different configuration of the larynx in the two sexes, the change of voice in the male at puberty and following castration, etc., strongly suggest that the larynx and perhaps the entire respiratory tract are closely linked with the sex hormonal functions of the body.

Based on such considerations, the author treated 20 males afflicted with advanced bronchogenic carcinoma by a combination of deep roentgen therapy and progynon C. The roentgen therapy was carried out with 190 kv., 0.75 mm. Cu. plus 1 mm. Al filters, half-value layer of 1.2 mm. Cu, 5 ma., 40 cm. skin target distance, 25 r/min., 3–5 fields of 80–150 $cm.^2$, 75–100 r per field until a total dose of 2,000 r per field was reached. One exposure was given every day or, if the patient was too weak, every second day. From the beginning of the irradiation the patient also received orally a tablet of 0.05 mg. progynon C three times a week or, when there was too much swelling of the breast, twice a week. The administration of the progynon C was continued in one case for over a year without untoward effect.

A study of the results shows that the course of the disease in the advanced cases with marked cachexia could not be influenced by this combined method of treatment. Likewise, in the more localized cancers no notable reduction in the size of the primary tumor or the surrounding infiltration of the lung was obtained, but the general condition of the patient was definitely improved.

The author has used the supplemental hormone therapy in bronchogenic carcinoma for only a year. Therefore, he considers the present report as preliminary. The investigations will be continued and extended to other hormone preparations.—*T. Leucutia, M.D.*

Popp, Walter C., Bargen, J. Arnold, and Dixon, Claude F. Regional enteritis; roentgen therapy. *Proc. Staff Meet., Mayo Clin.*, Jan. 4, 1950, *25*, 1–5.

Surgical resection only partly answers the problem of therapy in regional enteritis; more and more patients return because of recurrent enteritis after apparently satisfactory wide resection of the diseased segment. Roentgen therapy was therefore tried in some of the cases of severe ileitis which had not responded well to surgical resection.

The therapy consisted of irradiation of four areas covering the whole anterior aspect of the abdomen with rays generated at 130 kv. and filtered with 6 mm. of aluminum. "The output was 135 r measured in air." (This quote is the only mention of quantity of radiation, so it seems that it is the dosage administered to each area.) The treatment was repeated at intervals of one month until at least three courses of treatment had been given.

In 20 of 43 cases followed long enough to be evaluated, results were very favorable; the patients became largely symptom-free and returned to their former occupations. Fourteen others were improved, 7 were not helped, and 2 died. Additional therapeutic measures included a high-protein diet, periodic courses of sulfathalidine, and other supportive measures.

Three case histories are cited.

These cases and other similar ones suggest definitely that while the active disease may be stayed, or at least interrupted, healing and subsequent cicatrization are likely to occur and this may or may not eventually lead to surgical treatment.—*H. G. Moehring, M.D.*

Nogales, F., and Bedoya, J. Tuberculosis del cuello uterino (7 casos) y su tratamiento radiológico. (Tuberculosis of the uterine cervix [7 cases] and its radiation treatment.) *Radiol. cancerol.*, Jan.–April, 1949, *4*, 93–104.

Tuberculosis of the uterine cervix is rare. It appears that the first case was published by Lisfranc in 1842 under the name of "scrofulous lesion of the cervix." Daurios in 1899 studied 24 cases of tuberculosis of the cervix and vagina which he made the basis of a thesis. Moore in 1919 estimated that 170 cases were reported in the literature up to that time. In 1935 Parrain collected a total of 260 cases which he reviewed in detail.

In Spain, Recasens published 1 case, López Dóriga 2 cases and L. Morillo 7 cases. To these the authors now add another group of 7 cases, 5 of which were selected from among 2,800 histories of patients afflicted with clinical tuberculosis and 2 on the basis of available biopsies. The incidence thus amounts to 0.25 per cent which is considerably higher than that given in the world literature (Collins, 0.00119 per cent; Norris 0.026 per cent, etc.). While Dietel and other investigators are inclined to attribute the higher incidence which is also observed in the Italian and Japanese women to climatic and racial factors, the authors believe that it is the result of the higher fertility of the women in the three countries, predisposing to tuberculous genital infection during pregnancy, parturition and the post partum period as well as in abortions. This is supported by the fact that although tuberculosis of the uterine cervix may occur at any age, it is encountered most frequently during the period of active sexual life, usually secondary to a lesion in the lung or in the lymph nodes.

The case histories of the 7 patients observed by the authors are presented in short résumés. As already mentioned, in 2 of these patients only the biopsies were available, in the other 5 the treatment consisted of Sturmdorf operation (1 case), streptomycin (1 case) and radium therapy (3 cases). The radium was applied intracervically and/or in contact with the cervix. In 2 cases one application proved sufficient but in the third three applications had to be made at intervals of about two months. The dose of the individual applications in all 3 cases varied between 720 and 1,680 mg. hr., nearly always given in twenty-four hours. The dose of streptomycin which was applied successfully in 1 case amounted to 25 grams.

The authors mention that Morillo obtained a cure in all his 7 cases from the application of radium which he occasionally employed alone, but most frequently combined with deep roentgen therapy and ultraviolet irradiation. In 1 case he used a dose of only 720 mg. hr., but in the others three or four times as large a dose was necessary, supplemented by roentgen and ultraviolet irradiation.

The authors do not endorse radical surgery (panhysterectomy), as recommended by Collins for the treatment of tuberculosis of the uterine cervix, except when the presence of other tuberculous or non-tuberculous genital lesions constitutes a more definite indication.—*T. Leucutia, M.D.*

Quastler, Henry. Radiotherapy of acne vulgaris; comparative tests of treatment technics. *Radiology*, Feb., 1950, *54*, 247–256.

The author used the "factorial design" method of evaluating quality of radiation, intervals between treatments and roentgen-ray dosages in the treatment of acne vulgaris. Within the limits tested, the rhythm of irradiation was shown to be the decisive therapeutic factor, while dosage and quality of radiation have no significant influence; 30 r is just as effective as 120 r. Divided smalls doses are more effective than single larger doses. In general, acne therapy can be done with smaller doses and shorter intervals than commonly used. A characteristic radiobiologic future of the acne response is discussed.—*E. E. Seedorf, M.D.*

Ward, G. E., and Hendrick, J. W. Results of treatment of carcinoma of the lip. *Surgery*, March, 1950, *27*, 321–342.

Two hundred and fifty-nine cases of histopathologically proved carcinoma of the lip were treated over a fifteen year period. In this series most lesions occurred in men (251 cases), usually on the lower lip (239 cases), and 38 per cent had associated precancerous lesions

such as keratoses, leukoplakia and chronic commissural fissures. Seventy-nine patients had received previous inadequate treatment, 73 with roentgen rays, radium, or both, with dosages ranging from a few hundred to 2,000 r.

The authors believe that adequate treatment of the primary lesion is of great importance in prevention of recurrence and/or metastases and that this is best achieved with surgery. Roentgen therapy, consisting of fractionated dosage over a ten to eighteen day period with unfiltered (and otherwise unspecified) irradiation to a total dose of 6,000–7,000 r was used in 69 cases with lesions less than 1.5 cm. in diameter and less than 0.5 cm. in depth, with 79 per cent five year cures. Radium or radon was not used because of previous experience where this modality in the authors' hands produced extensive sloughs and infection.

Surgical procedure in lesions less than 2 cm. in diameter and 1.5 cm. in depth consisted of V-shaped excision which included 1 cm. of normal tissue around the margins of the growth. With more extensive lesions, more radical excision with plastic procedures as necessary were used. In previously untreated cases, operation gave 89 per cent five year cures when used alone, and 51 per cent five year cures when used with irradiation. In those cases previously treated, operation resulted in a 64 per cent five year cure.

Routine neck dissection was recommended if the lesion was over 1.5 cm. in diameter and of histopathologic Grades 2, 3, or 4, even if no lymph nodes were palpable. For extensive metastases with fixed lymph nodes 3 to 5 cm. in diameter, irradiation to skin tolerance, with radon implantation if necessary, was recommended and this was followed by radical neck dissection. In lesions less than 3 cm. in diameter, of low histopathologic grade with no palpable lymph nodes present, routine dissection was considered inadvisable. Prophylactic irradiation was also considered inadvisable.

A marked relationship of histopathologic grade and metastasis to lymph nodes was found in 9 per cent of Grade 1 showing subsequent metastasis as compared with 55 per cent of Grade 4. Again in this series the relationship of curability to histopathologic grade was demonstrated, with 95.4 per cent three year cures in Grade 1 and 38.2 per cent in Grade 4.

The authors conclude that in their experience surgery gives between 10 and 12 per cent better five year cures than irradiation. The over-all five year non-recurrence in all patients was 70.1 per cent.—*Robert Emerick, M.D.*

Hobbs, Arthur A., Jr. Fetal tolerance to roentgen rays. *Radiology*, Feb., 1950, *54*, 242–246.

A pregnant patient with carcinoma of the breast was given roentgen therapy to the tumor bed, axilla and neck. Four months after conception 1,500 r was given to each of two pelvic portals for metastases to pelvis and a smaller dose was again given four months later. A normal male child was delivered by cesarean section. The child exhibited normal physical and mental development until last seen at sixteen months of age.

The author reviews the literature and agrees that the greatest danger of injury to the fetus is during the first five months of pregnancy.—*E. E. Seedorf, M.D.*

Ghersi, Julio A., and Fromm, Günther A. Consideraciones sobre el estudio y tratamiento de la acromegalia; presentación de tres casos operados. (Considerations of the study and treatment of acromegaly; presentation of three operated cases.) *Prensa méd. argent.*, March 24, 1950, *37*, 579–591.

The authors report 4 cases of acromegaly, 3 of which were operated upon and 1 treated by irradiation.

The case histories are presented in detail, together with the photographs, roentgenograms, visual field charts, and photomicrographs. The histopathologic examination in the 3 operated cases revealed eosinophil adenoma.

The average duration of symptoms prior to admission was six years and three months. All patients had marked thickening and induration of the skin with dilatation of the pores. There were marked alterations of the skeleton with enlargement of the sella turcica and considerable increase in size of the frontal and sphenoidal sinuses as well as of the mastoids and maxillae. In each case there was bilateral hemianopsia which definitely improved following the operation in 2 cases and in the irradiated case. There were sexual disturbances, and 3 of the 4 cases had a very definite cardiac enlargement. Less frequent findings were:

rheumatoid polyarthritis, polyuria, recurrent epistaxis, positive protein balance, and slight erythremia.

A review of the literature shows that diabetes occurs in 12 to 17 per cent and glycosuria in 25 to 36 per cent of all acromegalic patients. To express the relationship existing between the diabetogenic and glycotropic factors and the growth hormone, the authors determine in every case, before and after treatment, the blood sugar tolerance curves provoked by glucose, insulin and a combination of the two, and compare these with the levels of the inorganic phosphorus in the plasma and of the growth hormone (gonadotropic hormone, 17-ketosteroids and corticotropic hormones). They also perform periodical check-up roentgen examinations of the osseous skeleton.

In regard to the surgical techniques, one of the authors (Ghersi) proposes that a 10 per cent solution of formol be applied for thirty minutes in the tumor bed following the excision of the adenoma so as to destroy possible residual cells and thus prevent a recurrence.

The roentgen therapy in the 1 case treated by irradiation was carried out with penetrating rays administering a total dose of 6,950 r in 33 seances through two portals.—*T. Leucutia, M.D.*

Sievert, Rolf M. A roentgen apparatus for intense roentgen radiation of short duration intended for biophysical research work and for special treatment purposes. *Acta radiol.*, March-April, 1950, *33*, 328–343.

A description is given of the new high voltage laboratory at the Institute of Radiophysics in Stockholm. The equipment is constructed for experiments with a roentgen, tube designed for the following purposes: (1) the study of the biological action of intense irradiation of short duration, and (2) the therapeutic application of such irradiation. Arrangement has been made for concentrating the radiation on deep-seated tumors. There is a Cockroft and Walton cascade generator of 1.2 million volts, a condenser battery comprising 40 condensers and a roentgen tube or the use of anodes with very large radiating surfaces. The electron emission in the roentgen tube is produced by means of a large number of wolfram filaments which are fed with the current from a storage battery giving an effect of up to 200 kw. The emission current used has been of a magnitude of about 2,000 amperes.—*Mary Frances Vastine, M.D.*

Lindell, B., Sievert, R., and Wahlberg, T. A method of concentrating roentgen rays for deep therapy. *Acta radiol.*, March-April, 1950, *33*, 344–356.

In the preceding paper in *Acta radiol.* an account is given of the new high voltage laboratory at the Institute of Radiophysics of King Gustaf V's Jubilee Clinic, Stockholm. A new type of roentgen tube with a conical anode used to obtain an extremely high relative depth dose is incorporated in this equipment. The aim of future experiments is to construct a tube for a dosage distribution suitable for giving a high tumor dose, without destroying too much of the surrounding normal tissues.

The hot cathode used in this construction will give an electron emission reaching several thousand amperes. It consists of a number of filaments (at most 144) connected in parallel around the anode. The filaments are pure wolfram wires, each 12.4 cm. long and 0.05 cm. in diameter.

Investigations were made on the distribution of dosage from this tube and some preliminary results are reported. Isodose curves have been calculated and are compared with results from dose measurements. A depth dose of 160 per cent has been obtained 8 cm. from the surface in a masonite phantom at a discharge of 200 kv. (peak). An electron emission of 1,200 amperes makes possible an irradiation time of only 100 microseconds.—*Mary Frances Vastine, M.D.*

Hultberg, Sven, Larsson, Lars-Eric, and Eklund, Lennart. Some cases of radiation injury in radiologic work. *Acta radiol.*, March-April, 1950, *33*, 376–387.

The Institute of Radiophysics under the direction of the Royal Medical Board has supervision over all the establishments in Sweden in which radiologic work is done or where radioactive substances are stored.

The radiation injuries that have come to the notice of the Institute have been of two kinds; local injuries (chiefly skin injuries) and blood damage. The causes of the local radiation injuries are almost, without exception, brought about by faulty working methods. These are usually more easily determined than the causes

of blood damage. Injuries of a local nature are usually produced by circumstances which are known either by the injured person or somebody else. On the other hand, radiation injury which shows up as blood damage is the result of smaller, little noted insults which have extended over a long period of time. Blood damage differs from local injury in that the injured person is not made uncomfortable at the beginning and so may unknowingly continue to subject himself to injurious radiation.

Reports on 5 radiation injuries among radiologic workers and 3 among patients undergoing roentgen examination are given. The importance of adequate and rapid investigation of such cases in order to secure prompt execution of protective and other needed measures is stressed.—*Mary Frances Vastine, M.D.*

Smith, E. J., and Scharfe, E. E. The nasopharyngeal radium applicator in the treatment and prevention of deafness. *Canad. M. A. J.*, Feb., 1950, *62*, 150–156.

The authors emphasize that this form of treatment is not without potential danger and is not to be considered a substitute for adenoidectomy.

Deafness due to tubal obstruction frequently clears up under conservative therapy and this should be considered before employing any form of radiation therapy. If tubal inflation does not improve hearing it is not reasonable to expect improvement following irradiation. Improvement in hearing has been noted in many cases of lymphoid hyperplasia treated by irradiation.—*A. E. Imler, M.D.*

Portmann, U. V. Cancer of the breast. *J. Michigan M. Soc.*, March, 1950, *49*, 304–308.

Frequently women do not discover cancers in the breast before they are well advanced because it is difficult to detect small tumors even by careful palpation, especially in obese individuals. Also, some women delay having a physician examine them because they have no pain, they fear cancer, or for economic or other reasons. It has been found that delay in treatment may be attributed to the patient in about 65 per cent of instances. Delay in 25 per cent of instances also has been attributable to bad medical advice.

The treatment of cancer of the breast requires cooperation of the physician, surgeon, radiologist and pathologist. Surgeons and physicians should recognize the limitations of operations for cancer and radiologists be aware of the indications for operation. Classifications based upon clinical criteria alone are not satisfactory in deciding the indications and limitations of different methods of treatment on the basis of statistical results. Furthermore, classifications based on pathologic criteria alone are not satisfactory in deciding methods of treatment or comparing the results. Portmann presents a clinical and pathological classification,—in four groups or stages, depending upon the extent of involvement and the presence or absence of local and/or distant metastases. Undoubtedly the most satisfactory method of classifying cases of cancer of the breast is to weigh all clinical and pathological evidences of the extent of the involvement.

In many instances it will be impossible to differentiate clinically between benign and malignant neoplasms of the breast, and biopsy and microscopic examination of the tissues are necessary. While biopsy of small, localized, movable tumors of the breast by aspiration needle or similar methods is not always reliable, aspiration biopsies are satisfactory for confirming diagnosis in cases with frank clinical manifestations of cancer.

Approximately 25 per cent of all cases operated upon will be in stage 1, and the general average of five year survivals will be about 85 per cent by operation alone. Routine postoperative irradiation is unnecessary for stage 1 cases because the curability rate by operation alone is high, and postoperative roentgen therapy here has not increased the survival rate.

When only a few axillary nodes are found to be involved, perhaps 25 per cent of all, such cases may be classified in group or stage 2. About 25 per cent of cases operated upon will be in this category, with the general average of five year survivals less than 50 per cent by operation alone. Postoperative roentgen therapy should be given in group 2 cases, especially to the axilla and the clavicular region. Although this procedure may not cure, because cancers of the breast are inherently radioresistant, it will increase the five year survival rate of approximately 10 to 15 per cent of stage 2 cases. There is abundant experimental and clinical proof that irradiation may inhibit de-

velopment of cancer cells or destroy them and irradiated tissues resist their growth.

The five year survival rate is in direct proportion to the number of lymph nodes involved; therefore, patients with metastases in many nodes may be classified in group or stage 3. The general average of five year survivals after operation alone for such cases is not more than 15 per cent, but this can be increased by postoperative roentgen therapy in about 10 per cent.

Group or stage 4 includes patients who have remote metastases on initial examination. Also, included in this category are patients with palpable enlarged supraclavicular nodes, involvement of the opposite breast or contralateral lymph nodes, or clinical evidence of involvement of other viscera. Approximately 20 per cent of all cases in the author's series had evidence of remote metastases on initial examination. These cases are incurable. "criteria of incurability" are listed under the headings of *Skin*, *Breasts* and *Metastases*.

The only available method of proved efficiency in patients with such criteria are roentgen and radium therapy and endocrine therapy for palliation. Adequate irradiation of patients with incurable breast cancer will result in approximately 15 per cent five year survivals. Operations following irradiation for incurable cancer invariably have revealed neoplastic tissues still present in lymph nodes and a well fibrosed breast, and the author concludes that irradiation does not make patients with "criteria of incurability" surgically curable. Sterilization by roentgen irradiation may be considered a form of hormone therapy. It should be performed for all patients who still menstruate and show some "criteria of incurability" for those who have local recurrence or remote metastases. Progress of the disease seems to be delayed frequently enough to warrant sterilization as a routine procedure.

Many women with local recurrences, metastases from cancer of the breast or other incurable indications are benefited from administration of sex hormones. The results with stilbestrol are inconsistent, and best in women sixty years of age or older. Androgens seem to be more effective for young women and for patients with osseous metastases. Portmann has used testosterone propionate intravenously 100 mg. three times a week. The roentgenologic appearance of osseous metastases frequently changes with apparent new bone formation. In others, symptomatic relief may be obtained without change in the appearance of metastatic lesions.—*S. G. Henderson, M.D.*

Mayer, Léopold, and Mayer, Charles. L'adénocarcinome du corps utérin; considérations sur le diagnostic et le traitement. (Adenocarcinoma of the body of the uterus; diagnostic and therapeutic considerations.) *Acta chir. belg.*, Feb., 1950, *49*, 199–211.

This report concerns a review of 76 cases of carcinoma of the fundus observed and treated by the authors and their collaborators between 1940 and 1949. They note that during this same period there were 212 cases of carcinoma of the cervix and 11 cases of carcinoma of the ovary. Their experience is different from that of other authors who report cervical carcinoma 8 to 10 times more frequent than carcinoma of the fundus, since they themselves found cervical cancer only 3 to 4 times more prevalent. The age incidence in their series was thirty-nine to seventy-five years, with an average of 59 years. Approximately two-thirds of their cases supervened in menopausal women.

With respect to pathological anatomy, they distinguish between two forms: (a) diffuse, which is an extensive involvement, possibly invading all of the endometrium. Tumors may be polypoid or fungating, and, in advanced stages, infiltrate muscles, extend to the serosa and form nodules on the surface of the uterus. (b) The circumscribed form sometimes is restricted to a small part of the uterus, in which case curettement biopsy may remove the lesion entirely.

They accept Broders' classification of four grades of malignancy, and draw attention to the adeno-acanthoma, which is an association of squamous metaplasia with some adenocarcinomatous endometrial elements. In their opinion, only the adenocarcinomatous elements are important; the squamous elements do not contribute, of themselves, a factor of malignancy, although they do contribute to the disorderly histopathological picture.

They review the literature of predisposing factors and draw attention to the possibility that hormones may act on the endometrium as possible cancerogenic agents.

Chief diagnostic reliance is placed upon

biopsy curettage; smear techniques are more difficult with reference to fundus cancer than to the cervix cancer because of less differentiation of the cells in the former. They recognize that sometimes diagnosis of adenocarcinoma has been made when there have been no clinical signs and they also recognize the value of the method as a detection diagnostic procedure, but feel that diagnosis can only be established with certainty by biopsy curettage.

Their review of the literature with reference to therapy is rather extensive, the purpose being to compare the results of radiation therapy by radium and/or roentgen rays alone, or with those obtained in combination with surgery and by surgery alone. Of the authors' 76 cases, 54 were operated on between 1940 and 1945. Forty-nine of these had total and 5 had subtotal hysterectomy. One patient died of complications, 2 had abdominal metastasis at the time of operation and died three months and one year respectively, after the operation. Thirty-eight were reviewed after five years and their recovery was maintained. Three patients were lost to follow-up. Counting only the 50 cases known to follow-up, the authors claim 76 per cent survival.

They conclude that abdominal total hysterectomy gives favorable results with an insignificant operative mortality. Roentgen therapy and curie therapy are useful adjuncts, but they feel that total hysterectomy retains all of its value in the treatment of cancer of the body of the uterus.—*A. K. Wilson, M.D.*

Morris, John McL., and Meigs, Joe V. Carcinoma of the cervix; statistical evaluation of 1,938 cases and results of treatment. *Surg., Gynec. & Obst.*, Feb., 1950, *90*, 135–150.

In discussing the matter of surgery versus irradiation, the statement is made that radical surgery can be done safely with a good cure rate in selected cases. While the possibilities of surgery are being re-explored, the value of irradiation has been proved and this should be the treatment for cancer of the cervix except in institutions equipped for investigative radical surgery. The authors deplore the number of total hysterectomies being done under the guise of the radical operation for cancer of the cervix.

It is known that small doses of radium of about 1,500 milligram hours or less will not produce a cure and that very heavy doses, such as 10,000 milligram hours, will produce excessive damage to normal tissue. Between these two extremes there are a large number of values which produce inconsistent results. Sometimes severe complications occur with small doses and at other times large doses produce no effect on the tumor. The tumor radiosensitivity and the normal tissue radiosensitivity are, to date, unknown factors. The tumor dose of roentgen radiation is often far different from the calculated dosage. Isodose curves often show that the distal extensions of a given tumor do not receive a cancerocidal dose from the radium given. Then, of course, there is the difficulty of determining clinically the exact extent of the tumor.

A tremendous amount of work remains to be done in this field. At the present time irradiation is a relatively blind procedure. For this reason and because there continues to be evidence of radioresistant cases it seems worth while to advance and improve the technique of surgery as well.—*Mary Frances Vastine, M.D.*

Paterson, Ralston, and Tod, Margaret. The presentation of the results of cancer treatment. *Brit. J. Radiol.*, March, 1950, *23*, 146–150.

Certain attributes are necessary to an acceptable method of recording the results of treatment or control of cancer; it must be simple, straightforward, and without ambiguity; it must contain all relevant figures, including the selection of the sample and the actual statistical analysis; an agreed method of presenting percentage should be used; and agreed fixed reporting periods should be established.

Percentage survival rates have been determined on the net survival rate, by actuarial methods using the methods of life-table construction, and the crude survival percentage. The last is the method strongly advocated by the authors. It considers only those individuals known alive and the total number in the sample This gives a somewhat lower figure than the net survival rate, in which the individuals untraced and those dying of intercurrent disease are deducted from the total. In estimation of the crude rate, the process is much simplified,

and any possible conjecture as to the condition of the untraced patients is eliminated.

The authors advocate reporting results at three, five, and ten year periods. The third is included to permit evaluation of change of treatment or other special analyses.

Two other suggestions are made in the interests of a higher degree of standardization of reports If all patients as treated are registered and no sample would be considered acceptable unless it is made up from pre-registered cases, any unconscious selection of cases would be eliminated. Also, accuracy of records could be enhanced by the development of a group of auditors who would be available for examination of cancer records at periodic intervals.—*E. F. Lang, M.D.*

Keibl, Edwin, and Lötsch, Anny. Beobachtungen über eine kombinierte Colchicin-Röntgentherapie bei Leukämie. (Observations on a combination of colchicin and roentgen therapy in leukemia). *Schweiz. med. Wchnschr.*, March 4, 1950, *80*, 228–231.

After a brief review of the effect of colchicin on cellular division and presentation of 3 cases of chronic myelogenous leukemia treated by colchicin and radiation therapy (2 mg. of colchicin administered subcutaneously and then roentgen radiation given at the optimum time, when depression of the white blood count resulted from the colchicin, usually at about two hours after administration of colchicin), these are the conclusions: Because of its effect on young leukemic cells, colchicin renders such cells more sensitive to roentgen rays and thus heightens the radiation effect, on the one hand, and restores a measure of radiation sensitivity in refractory cases, on the other.—*H. G. Moehring, M.D.*

RADIOISOTOPES

Tucker, F. R. The use of radioactive phosphorus in the diagnosis of avascular necrosis of the femoral head. *J. Bone. & Joint Surg.*, Feb., 1950, *32B*, 100–107.

The incidence of avascular necrosis of the femoral head appears to depend upon the normal variations in the vascular pattern and also upon the severity of the vascular injury. It is possible that delayed vascular occlusion may play a part, but the vascular damage is usually sustained at the time of the original injury. It may, however, be increased by inadequacy of immobilization, violence of manipulation and by the effects of some forms of internal fixation. Tucker states that it is a striking fact that there may be a mass of avascular bone in the body without any means of distinguishing it clinically or roentgenographically from living bone. This is true particularly during the first few months after fracture of the femoral neck with vascular occlusion. There is no reliable clinical evidence as to the viability of the femoral head. The surgeon must wait for several months or even for several years before the fate of the head can be predicted with certainty.

The problem of securing a reliable indication of the vascularity of the femoral head within a few days after fracture was studied by the injection of radioactive phosphorus, a safe and readily available isotope which is a normal metabolite showing a tendency to accumulate in bone. It was used in the form of disodium phosphate in aqueous solution. Experimental work was first undertaken on rabbits, 50 microcuries being injected into an ear vein. Operations on the neck of the femur and ligamentum teres were performed before injection of the isotope. Complete details of the experiments are given in the article, including estimation of amounts of the isotope found in the excised heads, etc.

In humans the isotope was injected into the antecubital vein, the usual dose being from 150 to 200 microcuries. It is possible that patients who do not yet show clinical evidence of avascular necrosis of the femoral head may develop signs of it in future years. Tucker found it noteworthy that, in the early stage when the isotope was injected, the fractures united quickly when a closely comparable content of the radioactive isotope was found in the femoral head and the trochanter (with ratios of 1:1, 3:2, 2:1) and there was no clinical or roentgenographic evidence of avascular necrosis. On the other hand, when the ratio of isotope content between the femoral head and the trochanter was 1:16, or 1:10, there was undoubted evidence of avascular necrosis and in one case, where there was a ratio of 1:5, there was evidence of segmental necrosis.

The possibility of complications arising from the administration of radioactive phosphorus must be considered. It may depress the activity of the hemopoietic system but the dosage used

in the cases studied seemed to be much below the amount used to inhibit hemopoiesis. It is also believed that the dosage is below that needed to stimulate carcinogenesis. Drilling of the femoral neck and head may damage the bone sufficiently to impair the efficiency of the Smith-Petersen nail. Any instrument driven into the head in the posterosuperior quadrant, or into the fovealar region, may well injure the remaining patent vessels, but if these zones are avoided the investigation can be carried out safely.

The author hopes that the method will be investigated by others and that, if confirmed, it may become an accepted routine in the treatment of intracapsular fractures of the neck of the femur when the viability of the head is in doubt.—*R. S. Bromer, M.D.*

Reynolds, L., Corrigan, K. E., and Hayden, H. S. Early detection of cretinism and other diagnostic uses of radioactive tracers in infancy and childhood. *Harper Hosp. Bull.*, Jan.–Feb., 1950, *8*, 4–6.

By means of carrier-free radioactive iodine (I^{131}), the authors have studied 46 infants and children believed clinically to have disturbed thyroid function. Three of the children thus studied proved to be total cretins with no demonstrable functioning thyroid, and 14 evidenced hypothyroidism of varying degrees. The remaining patients had thyroid function of normal degree, but 2 of these were found to have a thyroid carcinoma, 1 a thyroglossal duct cyst, 1 a non-toxic nodular goiter, and 1 was a mongolian idiot. There were 4 diffuse toxic goiters discovered.

The most interesting group were those of very low thyroid function which would have probably developed cretinoid characteristics if they had remained undetected. It is believed that by the isotope technique described incipient cretinism can be demonstrated with certainty before its presence could be detected by the usual diagnostic methods.

The use of radioactive phosphorus (P^{32}) is mentioned as a diagnostic aid in brain lesions, malignant bone tumors and metabolic bone disorders.—*Harold Fulton, M.D.*

CHEMOTHERAPY

Kent, Leonard, and Reh, Edward P. Treatment of bronchogenic carcinoma with nitrogen mustard. *Dis. of Chest*, Feb., 1950, *17*, 190–201.

Methyl-bis-(B-chloroethyl) amine (nitrogen mustard) is a useful drug in the treatment of some cases of inoperable bronchogenic carcinoma. This is especially true if the carcinoma is anaplastic. Whether nitrogen mustard is more effective than roentgen therapy in the treatment of bronchogenic carcinoma remains to be evaluated. Ultimately nitrogen mustard therapy, like irradiation, proves ineffective. Ease of administration, availability in communities where irradiation may not be obtainable and absence of skin reaction are advantages of nitrogen mustard as compared to roentgen therapy. Methyl-bis is a useful drug, but is toxic and must be administered with care. Studies must be repeatedly made on the patient's blood to follow the state of the bone marrow.

The effect of HN_2 in 19 patients with histologically proved bronchogenic carcinoma are described. These cases were unsuitable for other forms of therapy. Seven of the 19 patients are still alive. Five of the 7 living have anaplastic carcinoma. A good effect was obtained in 2 patients having anaplastic carcinoma. One is still living nine months after three and one-half courses of nitrogen mustard therapy. The other patient is still living six months following two courses of HN_2. Both had superior mediastinal involvement with decrease in tumor size and symptoms following therapy.

Nitrogen mustard often resulted in decrease in the leukocyte count, and platelet count, but in no patient did serious complications arise as the result of these effects. Toxic manifestations of nausea and vomiting were observed in several patients following HN_2 administration, but the intensity of these symptoms varied greatly.—*E. J. McDonald, M.D.*

Alpert, L. K., Greenspan, E. M., and Peterson, S. S. The treatment of the lymphomas and other neoplastic diseases with nitrogen mustard. *Ann. Int. Med.*, March, 1950, *32*, 393–432.

Nitrogen mustard (methyl bis-betachloroethylamine hydrochloride) was used in the treatment of 52 patients with Hodgkin's disease, giant follicular lymphoblastoma, lympholeukosarcoma (Sternberg), reticulum cell sarcoma, chronic lymphatic leukemia, subacute

myeloid leukemia, sarcoidosis and various carcinomas.

The most important toxic effects were observed in the hematopoietic system, the most serious being thrombopenia and purpura. It was interesting to note that a white blood cell count of 2,000 per cu. mm. was not considered a contraindication for the use of nitrogen mustard therapy.

Favorable effects were observed in 3 patients with giant follicular lymphoblastoma, 2 with lympholeukosarcoma (Sternberg), and the majority of 27 individuals with Hodgkin's disease. Of the latter, nitrogen mustard therapy appeared to be most suitably indicated in the following clinical types of Hodgkin's disease: (1) widespread involvement which could not be treated adequately with roentgen therapy; (2) individuals with lymphadenopathy and marked constitutional symptoms (fever, weight loss, etc.); (3) those with fever but without demonstrable enlarged nodes; (4) patients with visceral involvement; and (5) terminal cases which have become "resistant" to roentgen therapy.

Irradiation was the treatment of choice in patients with relatively localized disease in the peripheral, mediastinal or retroperitoneal regions; with obstructive lesions about the spinal cord, biliary tract, ureters or great vessels; with bone involvement, and with fibrosing types of Hodgkin's disease.—*G. J. Culver, M.D.*

Lynch, J. P., Ware, P. F., and Gaensler, E. A. Nitrogen mustard in the treatment of inoperable bronchiogenic carcinoma. *Surgery*, March, 1950, *27*, 368–385.

Approximately 70 per cent of patients with carcinoma of the lung are beyond curative resection when first seen by the thoracic surgeon, and conventional radiation therapy has not produced satisfactory results. Use of the chloroethyl amines in carcinoma of the lung was first mentioned by Rhoads in 1946, and to the small number of cases already reported the authors add 60 patients with inoperable carcinoma of the lung who were treated with nitrogen mustard.

Since it was found that response to the drug varied greatly in individuals, in 23 of the 71 courses of treatment the dose recommended by the Committee on Growth of the National Research Council (0.1 mg. per kilogram of body weight repeated for four consecutive days) was exceeded. In these instances total dosage range from 16 to 180 mg.

Dosage was not definitely related to success in palliation even within the wide limits of 0.4 to 3.0 mg. per kilogram. It was the authors' impression, however, that if the standard dose fails to produce benefit it is worth while to continue treatment until there is definite decrease in the percentage of lymphocytes present in the blood count. This regimen will produce good results in some patients who have not responded to the standard treatment regimen.

Over 50 per cent of the patients showed slight nausea or vomited on one occasion as a reaction to the nitrogen mustard. Only 13 per cent experienced severe nausea and vomiting, and in 13 per cent there was loss of appetite for one to two weeks after termination of treatment. Leukopenia below 5,000 occurred in 27 per cent; in 17 per cent it fell to about 2,000 and 6 patients showed a true agranulocytosis. These recovered on folic acid and penicillin. The gastrointestinal upsets were not related to the dosage used, but anorexia apparently was, and depression of the white blood count was definitely related.

Following treatment subjective improvement was most marked, 69 per cent of the patients showing moderate to excellent relief of symptoms. Fifty-four per cent showed objective improvement but all improvement was temporary.

Objective improvement, chosen as the most reliable indicator of success, was present in 83 per cent of undifferentiated neoplasms, in 50 per cent of the squamous cell type, in 33 per cent of adenocarcinoma and in 11 per cent of epidermoid carcinomas. Thus the efficacy of nitrogen mustard followed in general the laws of radiosensitivity. This similarity was also observed in microscopic studies done before, during and after treatment in 11 cases. Morphologic cell changes occurred in all cases and appeared as early as twenty-four hours after the first medication. Changes were most marked in the epidermoid type of tumor and here an increased number of mitoses were seen. In the less differentiated tumors there was decrease in mitoses with less marked morphologic changes. Because of the difference in degree of reaction and degree of clinical response, it was thought that the changes seen in well differentiated

tumors were not necessarily fatal to the cell.

Prolonged survival time has not occurred but nitrogen mustard has produced good relief and comfort for many patients and has the advantage of systemic diffusion rather than local administration. The authors feel that the results justify further use of the drug for palliative treatment of inoperable carcinoma of the lung.—*Robert Emerick, M.D.*

Harrington, William J., and Moloney, William C. The treatment of multiple myeloma with urethane. *Cancer*, March, 1950, *3*, 253–271.

A detailed report is given of 11 cases of multiple myeloma treated with urethane. The drug was given by mouth in a syrup solution, gelseals and in coated tablets. The usual dose was 3–6 gm. daily but varied up to 12 gm. daily and was given every day when tolerance permitted.

The duration of the disease before treatment ranged from four months to 4½ years and of the therapy from two weeks to twenty-seven months.

Six of the 11 patients were clinically improved or clinically well. One patient died of intercurrent disease and 1 was in such an advanced state of the condition that adequate therapy could not be given. The remaining 3 cases were considered therapeutic failures. However, all cases experiencing pain were relieved markedly and this factor alone is considered a definite advantage over other forms of therapy. Likewise, weight gain, prolongation of life, improvement in anemia, reduction in abnormal serum proteins and supression of myeloma cell proliferation in bone marrow were prominent features. Roentgen bone changes showed no tendency to regression on subsequent films.

Gastrointestinal disturbances, such as nausea, vomiting, anorexia and epigastric distress were observed but were relieved in great degree by the use of gelseals and especially coated tablets. Serious leukopenia may also result from urethane administration but can usually be averted by frequent blood studies.

Experience with more cases is needed before an accurate evaluation of urethane therapy can be made. However, one may conjecture that remissions will be effected in chronic multiple myeloma with urethane treatment while the acute forms of the disease will not respond.—*D. E. Vivian, M.D.*

Rottino, Antonio. Effect of adenylic acid therapy upon pruritus due to Hodgkin's and other diseases. *Cancer*, March, 1950, *3*, 272–278.

The antipruritic action of adenylic acid was discovered inadvertently when it was administered in the hope of improving the general condition of patients with Hodgkin's disease but only relief from pruritus was obtained.

Profiting from this observation, the authors have administered muscle adenylic acid to 11 patients with Hodgkin's disease and pruritus. Moderate to complete relief was obtained in 7 patients with dramatic results in 4. Several of these successful cases were refractory to nitrogen mustards and roentgen therapy.

To adjudge further its antipruritic function, the investigators administered adenylic acid to 36 patients with diseases of varying etiologies with associated pruritus, either generalized or localized. Seventeen per cent of the patients in this series had no response, while the remainder received from one plus to four plus (arbitrary indices) relief. There was no association with the duration of symptoms and the degree of relief obtained. The abated symptoms lasted from three days to three months.

The sodium salt of muscle adenylic acid was given intramuscularly in doses of 20 mg. every hour for five hours, repeated for three consecutive days.

The authors believe that adenylic acid plays a role in the normal biochemical pattern of the body, and that the artificial supplement of this substance reverts an abnormal metabolic process (resulting in pruritus) to a normal one. The exact mode of action is unknown.—*J. Wilson, M.D.*

Futcher, Palmer H., and Massie, Edward. Agranulocytosis due to propylthiouracil. *Ann. Int. Med.*, Jan., 1950, *32*, 137–138.

A white female, aged forty-seven, sought medical relief for a mild hyperthyroidism seventeen years after a partial thyroidectomy for goiter. Presenting symptoms July 3, 1947, were tachycardia, tremor, ocular lid lag and slight enlargement of the right lobe of the thyroid. Basal metabolic rate average plus 18 per cent, blood count normal.

Treatment with a 6-N-propylthiouracil 50

mg. five times daily by mouth and phenobarbital 30 mg. three times daily was prescribed July 10, 1947. The patient failed to follow instructions to return each week for blood count and basal metabolism and was not seen in until September 9, 1947. She had continued the medication through August 15, 1947, and at that time noted a nasal obstruction and occipital headache, On August 26, 1947 she, on her own initiative, reduced the dose of propylthiouracil from 250 mg. to 200 mg. daily and discontinued it entirely on September 6, 1947, because of the development of a sore throat. She entered the hospital three days later with temperature elevation, red throat with patches of exudate and cervical adenopathy. The white blood cell count was 4,500, with differential count 1 per cent eosinophils, 3 per cent myelocytes, 6 per cent juvenile polymorphonuclears, 39 per cent lymphocytes, and 50 per cent monocytes. Later counts revealed a further drop in polymorphonuclears to 1 per cent, and a rise of monocytes to 56 per cent. Throat culture revealed beta hemolytic streptococci.

Diagnosis of agranulocytosis was made and prognosis was thought to be fair because of the monocytosis.

There was prompt response to penicillin and folic acid by mouth. The patient was afebrile on the fifth day. The white blood cell differential quickly returned to normal and the patient was discharged on the tenth hospital day feeling quite well. The basal metabolic rate was then considered normal.

The authors admit this single case to be valueless in determining the incidence of agranulocytosis in propylthiouracil therapy. It is the only one of 27 cases treated by them that developed agranulocytosis.—*Harold O. Brown, M.D.*

Kennedy, B. J., Nathanson, I. T., and Aub, J. C. Ethyl carbamate (urethane) in the treatment of mycosis fungoides. *Cancer*, Jan., 1950, *3*, 66–73.

Mycosis fungoides, although sometimes controlled for considerable periods by roentgen therapy, may become refractory or too extensive for such therapy. Nitrogen mustards and antimony preparations show some promise in further treatment.

The influence of urethane (ethyl carbamate) on the clinical course of 9 patients is reported. In 4, there was definite improvement consisting of relief of itching, regression of tumors and epithelization of ulcers. There was histologic evidence of decrease of the cellular infiltrate. Initial remissions lasted from three to nineteen months. The disease becomes refractory to repeated courses of urethane.

Side effects of nausea, anorexia, vomiting, diarrhea, drowsiness, hematuria and albuminuria were noted. Leukopenia was not encountered. Glomerulonephritis is postulated as a possible toxic effect of urethane on humans.—*J. A. Campbell, M.D.*

MISCELLANEOUS

Engelstad, Rolf Bull, and Rennaes, Selmer. Attempts at gastric examination by photofluorographic methods. *Acta radiol.*, Jan., 1950, *33*, 49–56.

Photofluorographic equipment supplied with only a 30 ma. roentgen tube has enabled the authors to take adequate photofluorographic films of up to 30 individuals per hour (90 exposures). Roentgenographic evidence of gastric lesions was revealed in 8 patients.

In conventional roentgenographic examination much stress is placed on screening, palpation and adequate positioning. The photofluorographic methods break with conventional principles. However, by this method two, three or more films can be taken in different positions and, if necessary, with different amounts of contrast medium. In most instances such a series yields some information as to whether the contour is soft and elastic. Control roentgenograms were necessary, however, in several cases.

The advantages of the photofluorographic process are: (1) it can be performed quickly; more than 30 patients can be examined in an hour if not more than three films per patient are made; (2) the initial cost of the film is very small, approximately 15 cents for three exposures; (3) the operation of the unit is quite simple and does not require the services of a trained physician. If it is provided with a photoelectric cell, the unit can be operated by anyone.—*Mary Frances Vastine, M.D.*

Updegrave, William J. An improved roentgenographic technic for the temporomandib-

ular articulation. *J. Am. Dent. A.*, April, 1950, *40*, 391–401.

The difficulties of satisfactory roentgen examination of the temporomandibular joint are pointed out. Scattered radiation is indicated as one of the chief causes of poor definition. The use of a relatively small lead diaphragm is suggested. The aperture measures 1¼ inches in diameter, for use with a 10 inch target-film distance. The short distance produces distortion of the opposite side structures to such a degree as to render them practically indistinguishable on the roentgenogram. An aluminum filter of 1 mm. thickness is suggested because of the increased intensity of radiation. Slow speed high definition screens may be used because of the relatively high output.

The suggested positioning is as follows: cassette angled 15° toward feet, side of mandible flat against the cassette, central beam directed ½ inch anterior to and 2½ inches above the external auditory meatus of the opposite side. Accessories for positioning are described. Illustrations show uniformly good detail.—*C. N. Borman, M.D.*

Braibanti, Tullio, and Prevedi, Giorgio. La tomografia nelle osteomieliti. (Tomography in osteomyelitis.) *Ann. radiol. diag.*, 1950, *22*, 114–136.

The authors have found tomography very useful in the study of bone infections. This was especially true in cases in which routine films failed to show details of the various structures of the bone due to sclerosis of the cortex or periosteal thickening.

A Grossmann-Chaoul type of apparatus was used with fixation of the patient and motion of the tube and film. Details of the technical factors are included in the article. This method proved especially valuable in the detection of small sequestra, and fistulous tracts and cavities which could not be visualized on routine films. They demonstrate the advantages of this method in cases of acute and chronic osteomyelitis, Brodie's abscess and infected fractures.

It appears that tomography is definitely indicated in cases of bone infection that respond poorly to treatment and also in those cases in which the roentgen diagnosis remains questionable. The illustrations that accompany this article are convincing.—*P. E. Russo, M.D.*

Sissons, H. A. Microradiography of bone. *Brit. J. Radiol.*, Jan., 1950, *23*, 2–7.

Microradiography as done by Barclay has been adapted to thin sections of bone. The bone is fixed in formalin, and following freezing in alcohol and solid carbon dioxide, it is cut into sections about 2 millimeters thick on a band saw. Single films and stereoscopic pairs are made and inspected with a binocular dissecting microscope. Examination of sections of growing bone, developing periosteal bone, sarcoma developing in Paget's disease, normal bone in a vertebra, and fibrous dysplasia shows that this method aids in demonstration of the normal and pathological structures supplementing conventional radiography and microtome sections.—*E. F. Lang, M.D.*

Hodges, P. C., Jenkins, R. T., and Williams, S. F. An improved x-ray phototimer. *Radiology*, Jan., 1950, *54*, 64–73.

The recent availability of well-insulated phototubes has made it possible to redesign roentgen-ray phototimers, making use of a circuit abandoned by Morgan several years ago because of inadequate insulation of the phototubes then available. In this circuit, the ninth dynode of the multiplier phototube is used as the output electrode, permitting elimination of the amplifier and polarity inverter formerly used. A hot cathode thyratron is substituted for the cold cathode tube. Other changes include improvements in high voltage supply, introduction of a resistor to compensate for inherent lag in the opening time of the roentgen-ray contactor, and elimination of the kilovolt compensating circuit which was found unnecessary. Impedance and shielding of critical circuits has been improved. Simplified schematic and detailed circuit diagrams of the new circuits and the phototimer are included.—*H. P. Brean, M.D.*

Kemp, L. A. W. An improved dose calculator for linear radioactive sources. *Acta radiol.*, Jan., 1950, *33*, 17–30.

A linear radium source dose calculator for screened sources was described earlier and now modifications and additions to the original scheme have been made.

The calculator is made up of a scale model which reproduces the geometry of the source relative to the point at which the dosage rate

is to be calculated. (The source may consist of up to 3 screened components in tandem.) The position of the source relative to the point at which the dosage rate is required may be varied at will by means of direct reading distance scales and convenient propelling mechanisms. In its new form the calculator indicates the actual dosage rate in roentgens per hour on a microammeter fitted with a special scale. Thus, once the instrument has been set up for the study of a given source all that the operator has to do is to position correctly that part of the model representing the source in relation to the series of points at which the dosage rate is required and note down the answers shown on the meter. In fact, the instrument simulates a radioactive source, the strengths and lengths of whose components may be varied at will, combined with a direct reading dose meter for exploration of distribution. The operational procedure requires no mathematical skill and at the London Hospital dose distribution calculations of relatively complex arrays, such as those associated with volume implants, have been left in the hands of radiography students working in the Physics Departments as part of their training.—*Mary Frances Vastine, M.D.*

Eaton, Robert M. Pulmonary edema; experimental observations on dogs following acute peripheral blood loss. *Dis. of Chest*, Jan., 1950, *17*, 95–101.

The author offers experimental evidence to explain the plumonary edema frequently seen postoperatively Experiments were carried out on dogs with observations made at varied intervals after loss of 25 per cent blood volume. By desiccation analysis, it was found that there was an initial rise of pulmonary moisture in the first twenty minutes following hemorrhage, with a drop below normal forty-five minutes after blood loss. A second rise occurrred one and one-half hours after blood loss, after which there was a gradual leveling off to normal at four hours. These changes were accompanied by elevation of pulmonary artery pressure and increased hematocrit concentration. In another series of experiments, it was demonstrated that lymph flow in the pulmonary lymphatic duct was doubled in volume forty-five minutes following hemorrhage, with gradual return to normal. On examination of the lungs, areas of patchy hemorrhagic infiltration and tissue and alveolar edema with vascular congestion were demonstrated. It was shown that these changes might persist for as long as five days. Further experiments on the administration of intravenous fluids demonstrated that this procedure caused still greater increase in pulmonary moisture, the pulmonary edema being more pronounced with physiologic sodium chloride than with either plasma or blood.

The author explains these changes as due to slowing of the circulation as the result of the rapid fall in vascular pressure with resultant sudden production of circulatory anoxia. This anoxic state in turn causes damage to endothelium with greater permeability of the capillaries and transudation of fluid to the tissue spaces and alveoli. The pulmonary congestion and edema produce a pulmonary block to normal circulation with resultant rise in the pulmonary artery pressure and peripheral venous pressure. In addition, two further factors act in producing acute pulmonary edema; (1) deep breathing, which accompanies the anoxic state causes an increase in intra-alveolar negative pressure; (2) in accordance with the laws of the flow of fluids through tubes, velocity is inversely proportional to cross section and lateral pressure is inversely proportional to the velocity. An increase in the circulatory pressure results from the decreased flow through the lungs and this tends to force fluids out of the blood vessels, thereby augmenting the sucking effect of the intra-alveolar negative pressure.

From a practical point of view, these experiments have a bearing on the employment of intravenous therapy postoperatively. In view of these findings, it is logical to conclude that care must be used in administering intravenous fluids to the elderly and poor-risk patients requiring radical surgical procedures with major blood loss. Necessary fluids should be given slowly and venous pressure should be watched closely. Abrupt elevation of blood volume by the use of too rapid administration of intravenous fluids may damage or overwhelm the lungs and subsequently produce cardiac failure through venous overload.—*L. K. Sycamore, M.D.*

Babkin, B. P., and Speakman, T. J. Cortical inhibition of gastric motility. *J. Neurophysiol.*, Jan., 1950, *13*, 55–63.

This experimental study was undertaken to

elucidate reported intra-abdominal sensations, eructations and a desire to defecate from electrical stimulation of the cortex of the brain and to determine the localization of cortical representation for gastric motility and autonomic phenomena in the dog. The authors performed 20 experiments on fasting dogs, under chloralose and urethane anesthesia in 14 and under dial, nembutal, pentothal and ether alone or in combination in the rest. Balloons were placed in either the pyloric antrum and/or the fundus through an incision in the anterior abdominal wall and the excursions of a closed air system were recorded on a continuous ink-writing kymograph. Simultaneous records were made of blood pressure, respiration, and occasionally of intestinal motility. The entire cortex of the exposed hemisphere of the brain was explored with bipolar silver wire electrodes of 2–3 mm. separation.

As a result of these studies, it was found that inhibition of pyloric antral motility occurs from the "insular-orbital" region and the subgenual portion of the anterior cingulate gyrus. No augmentation of antral motility was produced in this series by stimulation anywhere on the exposed cortex. A functional relationship between the orbital surface and the anterior cingulate gyrus is suggested, and the phylogenetic relationship of part of the "orbital surface" of the dog to the Island of Reil in man is pointed out.—*K. K. Latteier, M.D.*

Dragstedt, Lester R., Woodward, Edward R., Neal, William B., Jr., Harper, Paul V., Jr., and Storer, Edward H. Secretory studies on the isolated stomach. *Arch. Surg.*, Jan., 1950, *60*, 1–20.

In 1930, Dragstedt and Ellis reported that dogs whose stomachs had been totally isolated with perservation of the vagus nerve supply secreted from 1,000 to 2,600 cc. of gastric juice in a twenty-four hour period. Death in five to eight days occurred from progressive hypochloremia and dehydration, but life could be maintained many months by the daily intravenous administration of 2,000 to 3,000 cc. of Ringer's solution.

In 1932, Webster and Armour reported that 2 dogs, in which the stomach had been detached from the duodenum but not from the esophagus, secreted only 270 to 560 cc. of gastric juice when fed via the duodenum. Death did not occur. Later, Ivy and Grossman, with similarly prepared dogs, confirmed the findings of Webster and Armour.

Dragstedt and his co-workers now report further observations. They used dogs prepared as follows: (1) preserving the blood and vagus nerve supplies of the stomach, the terminal end of the esophagus was anastomosed end-to-end to the first portion of the duodenum or to the side of the first portion of the jejunum; (2) as in 1, except that the esophagus was anastomosed to the antrum of the stomach (leaving the fundus and body of the stomach isolated); and (3) the stomach or a part was isolated as in 1 and 2, the gastric blood supply was preserved but the vagus nerves were divided. In each animal, a cannula was inserted into the isolated portion of the stomach through a stab wound in the abdominal wall. A rubber balloon to prevent loss of gastric juice was attached to the cannula and supported in a canvas apron worn by the animal at all times.

When the only salt supplied is that in the diet, the continued secretion and loss of gastric juice resulted in death in from four to twelve days from progressive hypochloremia and dehydration. But life was preserved for long periods by the intravenous administration of 1,000 to 2,000 cc. of normal saline solution daily or by the addition of 10 to 15 gm. of sodium chloride to the daily diet. Cessation of salt replacement even after five or six months was followed by prompt death.

As hypochloremia and dehydration were allowed to develop, the volume and acidity of the gastric secretion dropped rapidly, but rose promptly when salt was given by vein or mouth.

With adequate salt and fluid replacement, both volume and acidity were but slightly reduced by fasting, in striking contrast to the reduction observed in Pavlov pouch dogs or in animals with vagal denervation of a total pouch.

To secure accurate data, repeated collections from a single animal were necessary because of the large daily variation. As an extreme example, one animal secreted 3,245 cc. of gastric juice one day, only 260 cc. the next.

When the entire stomach was isolated, the maximum average daily secretion was from 900 to 1,000 cc. When the fundus alone was isolated and the esophagus anastomosed to the

gastric antrum, the maximum average secretion jumped to 1,687 cc. Evidently, the antrum, when in contact with food, is a more powerful stimulator of gastric secretion than any other part of the gastrointestinal tract. This finding would seem to explain the discrepancy between Dragstedt's results and Webster's and Ivy's.

A drawback to the use of vagally innervated isolated stomachs in the study of gastric physiology is the great frequency with which progressive peptic ulcers appear. However, interest in this observation is heightened by the fact that no ulcers have developed in the denervated isolated stomach or pouch. The most obvious explanation would be that the gastric secretion, with the vagi intact, is much greater —further evidence that pure gastric juice has the capacity to digest all living tissue, including the wall of the stomach itself.—*George Cooper, Jr., M.D.*

Rosenthal, Sol Roy, and Elmore, Francis H. Studies on the contagiousness of coccidioidomycosis. II. The fate of spherules in sputum exposed out of doors. *Am. Rev. Tuberc.*, Jan., 1950, *61*, 95–105.

As the result of an investigation made on the fate of spherules in sputum exposed out of doors under varied conditions, it was found that the vegetative form of *Coccidioides immitis* develops out of doors, especially in earth, and the spherules were seen most frequently in specimens kept in the shade without earth. The vegetative form was rarely seen after thirty days, but the parasitic or spherule phase was evident up to 240 days. The viability of the spherules was of low order in this experiment, but the authors felt that this might be at least partly due to the fact that many of the sputum specimens used for the experiment were from a patient who was definitely recovering from the disease, and this may have influenced the viability of the spherules from this patient.—*Lois Cowan Collins, M.D.*

Rosenthal, Sol Roy, and Elmore, Francis H. Studies on the contagiousness of coccidioidomycosis. III. Infection in guinea pigs by contact with diseased animals. *Am. Rev. Tuberc.*, Jan., 1950, *61*, 106–115.

An experiment regarding the contagiousness of coccidioidomycosis was conducted with guinea pigs. Since it is generally believed that in humans the disease is initiated in the respiratory tract in most instances, the guinea pigs were infected intratracheally in order to simulate the conditions in humans.

The authors state that these studies are preliminary, and relatively few animals were used. Ten of 13 normal animals housed in four separate cages with infected animals presented evidence of infection after 46 to 175 days of contact.—*Lois Cowan Collins, M.D.*

Prehn, Richmond T. Note on the lack of progressive growth of metastatic mammary carcinoma transplanted subcutaneously into foreign strains of mice. *J. Nat. Cancer Inst.*, Feb., 1950, *10*, 893–894.

Greene and Newton deducted from studies on the evolution of cancer of the uterine fundus in rabbits that with complete development of a tumor, dependence upon the host animal ceases and that the tumor becomes autonomous. Using the technique of intraocular transplantation, they found that autologous transfer of early mouse tumors and homologous transfer of these tumors to members of the original strain were invariably successful, whereas transfer to alien strains and guinea pigs was unsuccessful. However, after complete tumor development (with metastases), transplantation to alien strains or to guinea pigs was readily effected.

The author used the primary tumors and metastatic nodules from an inbred strain of mice and transplanted them into the axillae of test mice of other inbred strains. The animals were kept until moribund to allow for the greatest degree of tumor development. Only primary tumors and metastases large enough for histologic section and transplantation were used.

After four to six months of observation in each animal, only 1 case in 76 test mice showed progressive and continuous growth. Here the growth appeared to be attenuated and four months after inoculation, microscopic study revealed tumor tissue resembling the original transplanted material. In all the other test mice, a small mass was palpable at the site of inoculation for three to five days after which it disappeared. In all of the control animals, the tumor transplants caused a fatal outcome.

The author concludes that mammary tumors which had metastasized (or their metastases) very rarely have the ability to grow progres-

sively in foreign strains of mice.—*K. L. Krabbenhoft, M.D.*

Morrow, Patrice L., Bierman, Howard R., and Jenkins, Robert. Effect of ultrasonic vibration on the formed elements of blood from normal and leukemic subjects. *J. Nat. Cancer Inst.*, Feb., 1950, *10*, 843–858.

Although the fragility of erythrocytes to numerous adverse physicochemical agents has been determined, little is known concerning the fragility of leukocytes to such agents. In this carefully controlled study, the authors employed an ultrasonic vibration of 635 kilocycles per second to show the reactions of heparinized blood from 30 normal and 15 leukemic subjects to this physical agent. The destruction time of 50 per cent of the cells (DT_{50}) in a given specimen was used as a basis for comparison.

It was found that the erythrocytes and leukocytes of blood from normal and leukemic subjects were destroyed at a logarithmic rate. Further, they demonstrated a significantly greater resistance to the effects of the ultrasonic vibration in leukocytes of lymphatic and myelogenous leukemia than those in normal blood. Only the major cell type involved in leukemia shows this increased resistance. The cells of chronic leukemia have a longer DT_{50} than those of acute leukemia. The erythrocytes from normal and leukemic subjects showed an unappreciable difference in DT_{50}. Younger cells were more resistant to the vibration, especially where the early form was the predominant type.

The lethal effects of ultrasonic vibration are attributed by one investigator to a mechanical force involving explusion of a dissolved gas from the medium. Others attribute these effects to coagulation of the protoplasm, or violent agitation produced intracellularly by increased pressure changes.

The effects noted in each type of leukocyte are recorded but offer no basis for definite conclusions other than those mentioned. A detailed description of the changes occurring within the cells in this study is also given. The possibility of a longer survival time of leukemic leukocytes in the circulating blood, based on the observations of this study, is regarded as purely speculative.—*K. L. Krabbenhoft, M.D.*

Ragaglini, Giorgio, Cardioangiografia sperimentale mediante puntura diretta del cuore. (Experimental angiocardiography by direct puncture of the heart.) *Ann. radiol. diag.*, 1950, *22*, 140–148.

The author briefly reviews the literature on this subject and then reports his results using the method on rabbits and dogs. The substance employed was uroselectan B, injected at the rate of 1 to 1.5 cc. per second, for a total of 4 to 8 cc. in the rabbit and up to 30 cc. in the dog. By this method the left ventricle, the thoracic and abdominal aorta and all of the main arterial branches can be clearly visualized.

He stresses certain points in technique which must be strictly adhered to. Thus the injection of the substance must be made at a constant rate and pressure to prevent acute dilatation of the heart. A substance of greater opacity and less irritation must be developed before this method of investigation can be used in clinical cases. Under accurate technical control the animals tolerated the procedure without any deleterious effects.—*P. E. Russo, M.D.*

Carrié, C. Zur Dosimetrie von Radiumträgern. (Dosimetry of radium containers.) *Strahlentherapie*, 1950, *81*, 595–598.

Various methods have been suggested to express the radium dose in r. Many institutes, including the author's, use the mathematical method specifying the dose for each given situation and type of applicator. This often necessitates complicated and time-consuming calculations.

To simplify the procedure, the author has introduced two practical devices which are described and schematically illustrated in the present article.

One device consists in the use of small celluloid plates with inscribed isodoses for radium needles of various size and strength. These are of value in determining the dose in r when needle containers are employed in one single plane, usually for surface application. The transparent celluloid plates corresponding to the radium needles of a given size and strength are superimposed on millimeter paper and the added doses for any point of the surface marked. If, for example, the isodose curve of 10 r/h of the first needle crosses the isodose curve of 3 r/h of the second needle, the added dose at this point will be 13 r/h. If many needles are used in close arrangement, the superimposed isodose curves may be difficult to read. In such instances celluloid plates of various colors are employed.

The other device was planned to determine the dose for more complicated situations when the radium needles are arranged in various planes and under different angles. The author made metal models of the various radium needles used. These models are somewhat longer than the actual radium needles or their active part and are pointed at one end. Fine wires which may be turned are fastened around their longitudinal axis. The isodoses are marked on the wires. Thus by placing the models in the position actually occupied by the radium needles, the intersection of two or several of the wires at a certain point will give the added value of the r/h at that point. This procedure, however, becomes quite cumbersome if too many needles have to be used. For such instances, the author constructed somewhat different models. Instead of fastening the wires around the axis he inserts them into a movable part of the metal needle which is provided with eyes at set distances. These model needles are stuck with their long-pointed ends into wax plates in an arrangement identical to that of the clinical application. The isodose marked wires are then inserted into the eyes of the movable part of the model needle and directed toward a given point. The added isodoses as indicated on the wires will represent the total dose in r/h at that particular point.—*T. Leucutia, M.D.*

Kunz, Heinrich. Über ein neues Schichtaufnahmegerät für Untersuchungen am stehenden, schräg oder horizontal gelagerten Patienten. (A new body-section roentgen unit for examinations in vertical, oblique and horizontal positions.) *Röntegn-Blätter*, March, 1950, *3*, 80–85.

The two types of body-section roentgen units used in Germany for the past fifteen years are the "planigraph" of Siemens used for body-section roentgenography and fluoroscopy with the patient in upright position and the "tomograph" of Sanitas for body-section roentgenography in the horizontal position.

An apparatus which combines these two features and can be operated also under various inclinations is described.

The unit, resembling in construction the planigraph, can be tilted from the vertical into the horizontal position, being mounted on a steel ring of about 2 meters diameter fixed to the wall and rotating on this ring as on a turntable. Both the tilting of the table and the movement of the roentgen tube are motor-driven. The range of the tube movement can be varied, thus changing the thickness of the layer represented.

Fluoroscopy with the moving roentgen tube helps to determine the depth of a lesion or a foreign body. If this is at the level of the axis of movement of the roentgen tube and the screen, no displacement of its shadow on the screen occurs, the displacement being proportional to the distance from this level. Single or serial body-section roentgenograms on the same film can be taken. The use of an additional table allows films to be taken with the effacing movement of the roentgen tube oblique or transverse to the longitudinal axis of the patient.—*Karol E. Matzinger, M.D.*

Berger, H. Ein neues vollautomatisches Serien- und Zielaufnahmegerät. (A new, fully automatic serial spot film device.) *Röntgen-Blätter*, March, 1950, *3*, 85–89.

The main features of this device are: (1) easy operation by the left hand; (2) quick transition from fluoroscopy to roentgenography with the screen locked automatically in position; (3) easy replacement of the cassette by one hand; (4) good access to the patient; (5) use of different film sizes.

The screen is moved by a handle on its left side, on which is a push-button operating the compressed-air driven movement of the cassette into exposure position, the electrical locking of screen and the exposure. With the push-button half depressed, the device is locked, after full depression the roentgen rays are switched off and the cassette is moved into exposure position. Then, the Bucky grid is set in movement; this in turn switches on the exposure of the film. When the button is released, the cassette moves back automatically in fluoroscopy position and the tube is energized for fluoroscopy.

The time from pushing the button to the exposure is constant and amounts to only 0.5 second. The whole operation is carried out by the left hand, the right being free for palpation and rotation of the patient.

The following cassettes can be used: 35 by 35 cm., 18 by 24 cm. and 13 by 18 cm. They can be exposed in both longitudinal and trans-

verse position; one, two, four and eight exposures on one film can be taken.

An ionization chamber timer, can be used for automatic exposure control.—*Karol E. Matzinger, M.D.*

Janker, R. Apparatur und Technik der Röntgenkinematographie zur Darstellung der Herzbinnenräume und der groben Gefässe (Angiokardio-Kinematographie). (Apparatus and technique for demonstration of the cardiac chambers and great vessels by roentgen cinematography (Angiocardio-cinematography).) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, March, 1950, *72*, 513–520.

The roentgen ray source is a constant potential generator, which is operated at 80 kv. and 20 ma. for plain films or at 90 kv. and 80 ma. for angiocardio-cinematography, and is capable of yielding 12 to 24 pictures a second. The examinations are done on a horizontal table, with the image of the fluorescent screen reflected into the camera by means of surface silvered mirrors. The table is so constructed that the image may be observed during the entire procedure, and also can be closely observed to guide cardiac catheterization. The camera shutter is adjusted so that 270° are open and 90° dark, and the tube is run for somewhat less than 75 per cent of the total time, taking advantage of the phosphorescence of the screen, and also producing sharper images because of less lagging of the previous image with each additional exposure.

An apparatus for making copies of the original film with each frame duplicated from 1 to 20 times, so that the resultant film will give slow motion effects, is also described.—*J. J. B. Light, M.D.*

Ardran, G. M. The pulmonary effects of toxic gases and smokes; an experimental radiographic investigation. *Brit. J. Radiol.*, Feb., 1950, *23*, 107–115.

A series of dogs was used to investigate the pulmonary effects of phosgene, chlorine, mustard gas, and the gas used to produce a smoke screen (hexa-chlorethane zinc oxide.) Mustard gas did not produce pulmonary edema, but bronchopneumonia developed after a few days. The other gases all produced pulmonary edema, and, through contraction of the smaller bronchioles, increase in lung volume. Clinical evidence of distress appeared before the roentgen changes, and the other laboratory findings, such as hemoconcentration, followed them. Slow development of edema is a good prognostic sign, but edema persists in any case longer than hemoconcentration. None of the animals which were allowed to recover developed bronchopneumonia, although histological evidence of bronchopneumonia was seen.

Comparison of the present findings with those of humans which have been exposed to gases shows that the effects are similar.—*E. F. Lang, M.D.*

Enersen, D. M., Woodward, E. R., Tovee, E. B., Neal, W. B., Jr., Sibley, J. A., and Dragstedt, L. R. Failure of vagotomy to prevent the formation of Mann-Williamson ulcers in dogs. *Arch. Surg.*, Feb., 1950, *60*, 223–232.

Seventeen animals with Mann-Williamson ulcers were subjected to complete gastric vagotomy and 13 with these ulcers were used as controls. The authors do not feel that there is a statistically significant difference in the survival times between the groups.

Since the purpose of gastric vagotomy is to abolish the hypersecretion of neurogenic origin in patients with duodenal ulcers and since the Mann-Williamson gastrojejunal ulcer is not of this origin, it is apparent that this animal preparation is not too well suited for evaluation of anti-ulcer therapy.

Cases of gastrojejunal ulcer in man somewhat comparable to Mann-Williamson ulcers in dogs are recalled from the literature. A case report is given showing the failure of complete gastric vagotomy to relieve a Mann-Williamson type of gastrojejunostomy ulcer. This patient had a posterior gastroenterostomy with an obstructed proximal jejunal loop; an entero-entero-anastomosis was done between the loops, thus diverting the duodenal secretions from the stoma, the vagus was divided. Physiologic tests indicated that a complete gastric vagotomy was done, but his jejunal ulcer which developed after the enteroentero-anastomosis, failed to heal or recurred promptly after temporary healing.—*S. H. Fisher, M.D.*

Forssberg, Arne. On the possibility of protecting the living organism against roentgen rays by chemical means. *Acta radiol.*, March-April, 1950, *33*, 296–304.

Studies of the effect of roentgen rays on enzymes containing the sulfhydryl group have disclosed that these enzymes are readily inactivated by roentgen rays in moderate dosage. By adding sulfhydryl-containing substances (cysteine and glutathione) to the irradiated enzyme solution, this inactivation effect can be counteracted.

Other workers have added to our information along these lines by injecting cysteine into rats and then irradiating them. The protective effects observed were most impressive. If the cysteine is given after the irradiation rather than before, it has no protective effect.

The author applied this principle of cysteine protection to animals by using epilation in guinea pigs as a criterion of the roentgen effect. He found that the cysteine injection given immediately preceding irradiation of the hair follicles protected them to a certain extent. Questions which remain to be answered include; "What is the quantitative relation between cysteine concentration and protective effect?" and "What interval between cysteine injection and roentgen treatment is the most suitable?" Another and most important problem to be investigated is, "Can even more serious damage be partly prevented by the cysteine treatment?"—*Mary Frances Vastine, M.D.*

Koletsky, Simon, Bonte, Frederick J., and Friedell, Hymer L. Production of malignant tumors in rats with radioactive phosphorus. *Cancer Research*, March, 1950, *10*, 129–138.

In studying the carcinogenic effect of P^{32} in rats, the authors employed a strain of adult white male rats which does not develop spontaneous bone tumors. Two experimental groups were used. The first group consisted of animals surviving a single LD_{50} dose of P^{32} (4.5 microcuries per gram of body weight), and the second of animals receiving repeated injections of P^{32} (1.5 microcuries per gram of body weight) every three weeks for a total dose of 9 or 12 microcuries per gram. The radioactive material was injected via the intraperitoneal route. Two groups of control rats, one receiving no radioactive material, and the other receiving 1 millicurie of I^{131} one year previously, showed no evidence of bone neoplasm. Complete necropsies, routine microscopic examinations of the femora and vertebrae and roentgen studies of the entire skeleton of most animals were done.

In those animals receiving a single dose of P^{32}, malignant tumors occurred in 9 of 19 rats, an incidence of 47 per cent. Since some of the rats were sacrificed or died prior to the average latent time for development of tumor, this figure may be low. The average latent period, or time of detection of tumor, in this group was 290 days. In the group which received repeated injections, 4 of 15 rats developed tumors, an incidence of 27 per cent. The average latent period in this group was 165 days.

Ten osteogenic sarcomas were seen, 4 in the jaw, 2 in the spine, 2 in the tibia, and 1 each in the femur and pelvis. Four of these tumors metastasized to the lungs. Three squamous cell carcinomas involving the face and associated with exophthalmos were also seen.

"Radiation osteitis" of varying degree occurred almost constantly in the femora and vertebrae of these rats, with or without sarcoma. The authors feel that there is strong presumptive evidence that these changes occur as a precursor to malignancy.

The production of malignant neoplasms by P^{32} is of interest in relation to the therapeutic use of this substance in humans, The LD_{50} dose of 4.5 microcuries per gram in the rat corresponds to 300 millicuries for a 70 kg. human, or about twenty times the usual therapeutic dose. It is not known whether smaller doses of P^{32} will produce malignancies in animals but very large doses of radioactive isotopes which deposit heavily in bone would seem to be contraindicated where long term human survival is to be expected.

Several roentgenographic reproductions and photographs of pathological specimens obtained from this study are used to illustrate the text.—*K. L. Krabbenhoft, M.D.*

Stevens, Charles D., Meinken, Mary Ann, Quinlin, Patricia M., and Stewart, Paul H. The distribution of radioactive iodine in mice with and without tumor 15091a after injection of radioactive sodium iodide. *Cancer Research*, March, 1950, *10*, 155–161.

The distribution of radioactivity in animals receiving a labeled inorganic iodide was determined for comparison with the distribution in animals receiving labeled organic compounds and the alterations occurring in the distribution of radioactivity in mice with mammary carcinoma, 15091a, are described.

It was found that the concentration of I^{131} in the sera of control and tumor-bearing mice was similar but the thyroid content was smaller in the mice with tumor 15091a implants than in the control mice. Higher concentration of the isotope in the spleen than in the blood of tumor-bearing mice was observed in some animals. This was apparently unassociated with splenic enlargement. Thymic gland concentrations in mice were higher than those found in rats.—*K. L. Krabbenhoft, M.D.*

Parker, H. M. Tentative dose units for mixed radiations *Radiology*, Feb., 1950, *54*, 257–262.

The original definition of the roentgen applied to roentgen radiation only. In 1937 a modified definition of the roentgen, based on the Bragg-Gray cavity principle of dosimetry, was adopted. Further forms of radiation require a new dose unit. Various units suggested are based on energy absorption or ionization per unit mass or volume.

The author recommends the adoption of a practical energy absorption dose unit called the rep, and defined so that "one rep represents an energy absorption dose in irradiated tissue of (exactly) 93 ergs per gram."

In mixed radiation exposures the author suggests the rem as a unit. This is described in detail.

The unit, roentgen, should not be discarded and will remain valuable for practical roentgen therapy.—*E. E. Seedorf, M.D.*

Herdman, J. P., and Jaco, N. T. The renal circulation in experimental hydronephrosis. *Brit. J. Urol.*, March, 1950, *22*, 52–55.

The authors produced an artificial hydronephrosis by severing the ureters in rabbits. At intervals of from one to sixty days later thorotrast was injected into the aorta through a carotid cannula. Angiograms were then made. The outstanding findings were that the blood supply was definitely decreased in these kidneys as compared to normal kidneys and that the longer the animals were allowed to survive the greater the decrease in dirculation appeared to be. Furthermore, it was noted that the opaque material was retained in the kidnys considerably longer in animals with hydronephrosis than in normal rabbits. From this the authors agree with others that it is quite probable that at least a part of the atrophy in kidneys in experimental hydronephrosis is due to ischemia. Particularly do they feel that this is true in relationship to the atrophy of the proximal convoluted tubule.—*A. J. Present, M.D.*